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AMERICAN SOCIETY FOR CIRCUMPOLAR HEALTH

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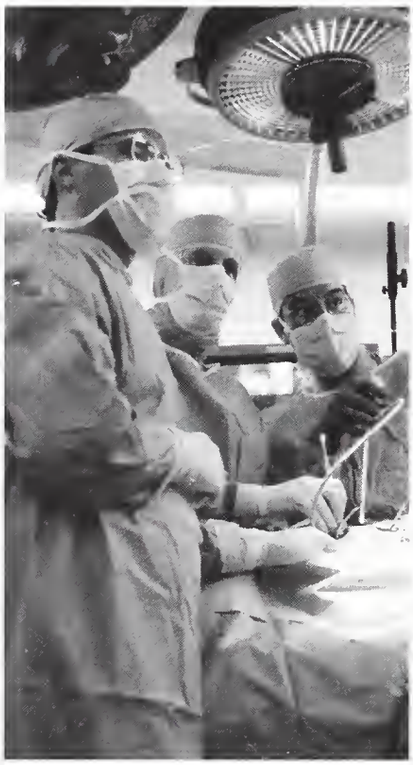

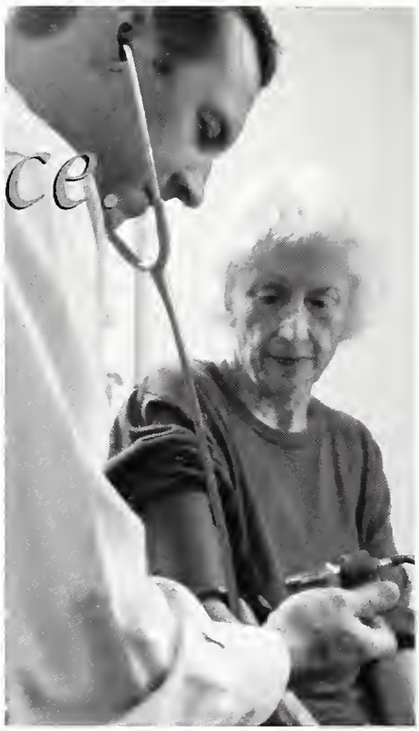

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About the cover: Brown Bear Mother and 3 cubs, Mikfik Creek, Alaska
Photo courtesy of Mark Newman, MD

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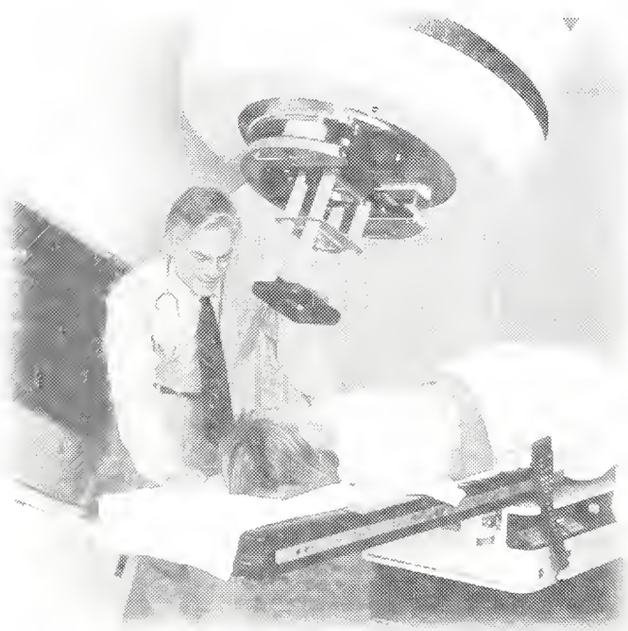

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PALINOPSIA WITH BACTERIAL BRAIN ABSCESS AND NOONAN SYNDROME

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Scott Wellman, MD[3]
Ed Crouch, MD[1]
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INTRODUCTION

Patients with traumatic, infectious, inflammatory or neoplastic processes affecting the visual pathways usually experience a loss of vision. Extra or additional vision may be associated with strabismus, ocular media disruption or macular irregularities. Extra formed images might be due to psychological disease but they can also be a result of seizures or the disruption of the processing of visual memory (1). We present a case with positive afterimages associated with a rare infectious central nervous system. disease.

CASE REPORT

A 19-year-old male with known Noonan Syndrome developed headache, dizziness and visual disturbance in July 1998.

The patient had previously received two detailed neuro-ophthalmic evaluations at the Ophthalmic Associates Cordova Clinic in 1993 and 1994 for a complaint of headache. He complained of a once weekly headache behind both eyes lasting about an hour. The headaches were not associated with changes in vision but felt better in cool air. His uncle had suspected a bulging of one eye. During those examinations, his visual acuity corrected to 20/25+ o with mild astigmatic correction. Confrontation fields and pupils were normal. He manifested a 6 distance and 8 near comitant exophoria without nystagmus. His irides were brown without Lisch nodules. Tonopen® pressures were 17 and 14 mmHg. Exophthalmometry was normal and symmetric. His anterior segment was normal. His optic nerve heads were cupped 0.5 o with a faint spontaneous venous pulsation present. The patient was given a presumptive diagnosis of vascular or migraine headache and no neuroimaging studies were ordered.

After an expedited referral from Cordova, the patient was examined and found to have normal distance visual acuity but a complete left homonymous hemianopia on confrontation testing and confirmed by Goldmann perimetry (Figure 1). He was referred to the Emergency Department. His necrologic exam was otherwise non-focal however he was febrile. An MRI was ordered after an emergent computed tomogram of his head revealed a ring-enhancing lesion in the right posterior parietal, occipital area (Figure 2).

The pulmonic stenosis and hypertension were evaluated as a part of pre-operative evaluation of a patient with Noonan syndrome. Echocardiogram showed moderate pulmonic stenosis consistent with his known fingernail clubbing and a secundum atrial septal defect with primarily left to right shunt.

The patient underwent craniotomy with drainage of a "foul-smelling" abscess. Gram stain revealed gram positive cocci and gram negative rods. Cultures grew out *Streptococcus anginosus group* sensitive to cefotaxime, penicillin G and vancomycin. An indwelling catheter was placed and the patient was started on ceftriaxone and metronidazole.

Post-operatively, the patient continued to recognize his hemi-field defect. In addition, he was able to

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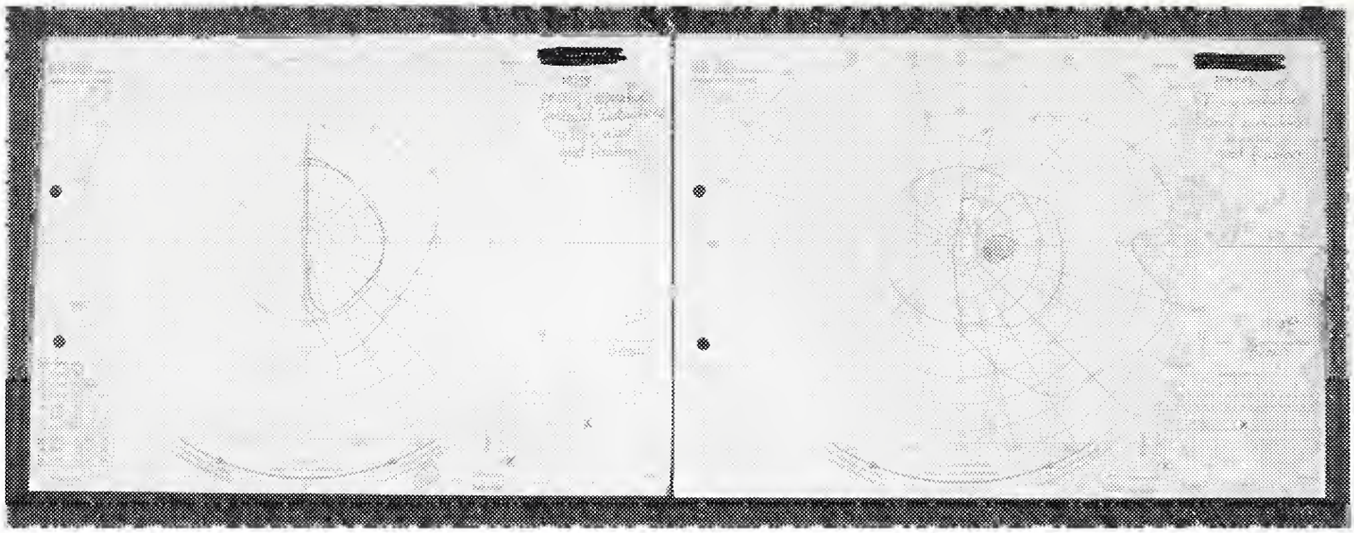


Figure 1. Goldmann Perimetry demonstrating complete left homonymous hemianopia pre-operatively.

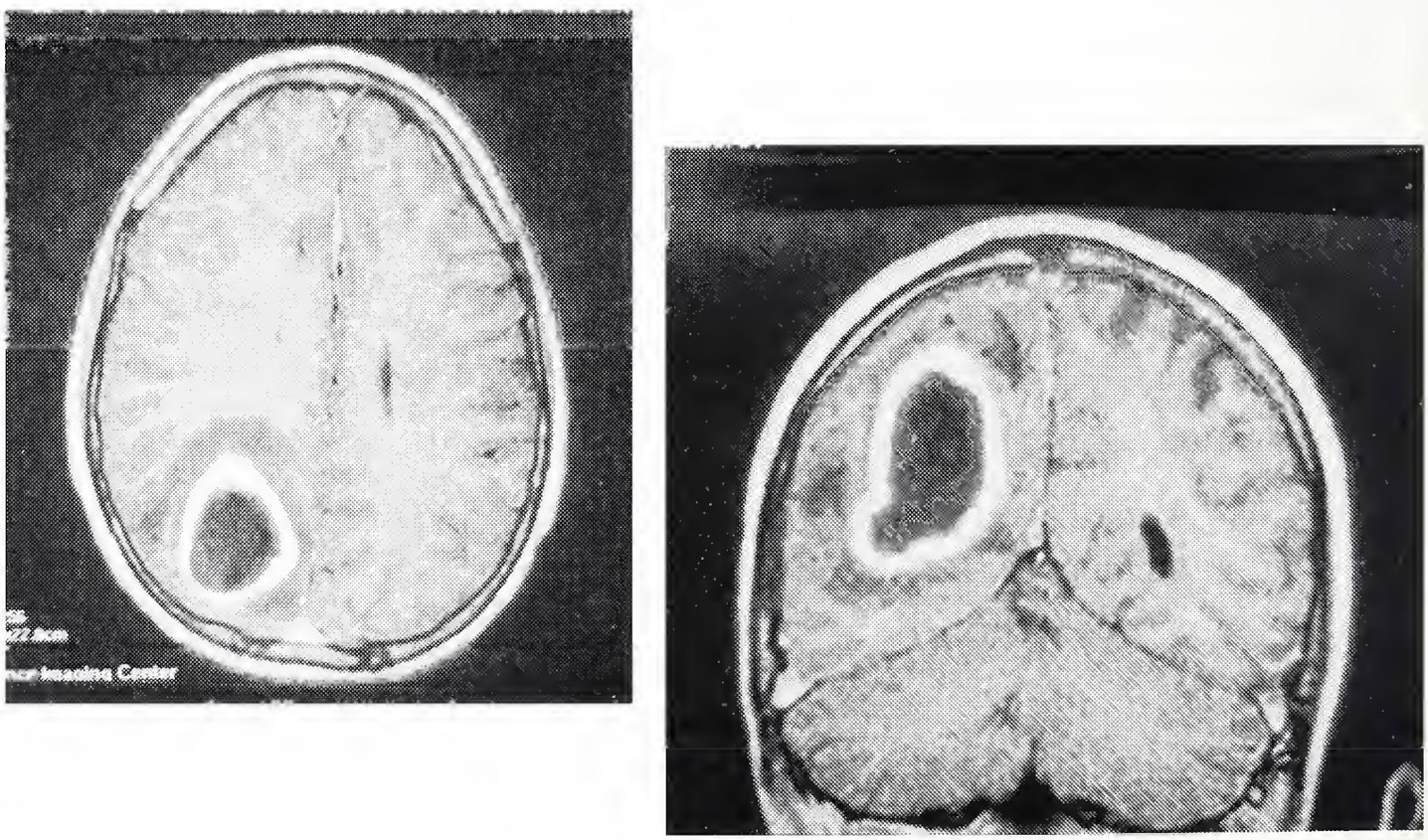
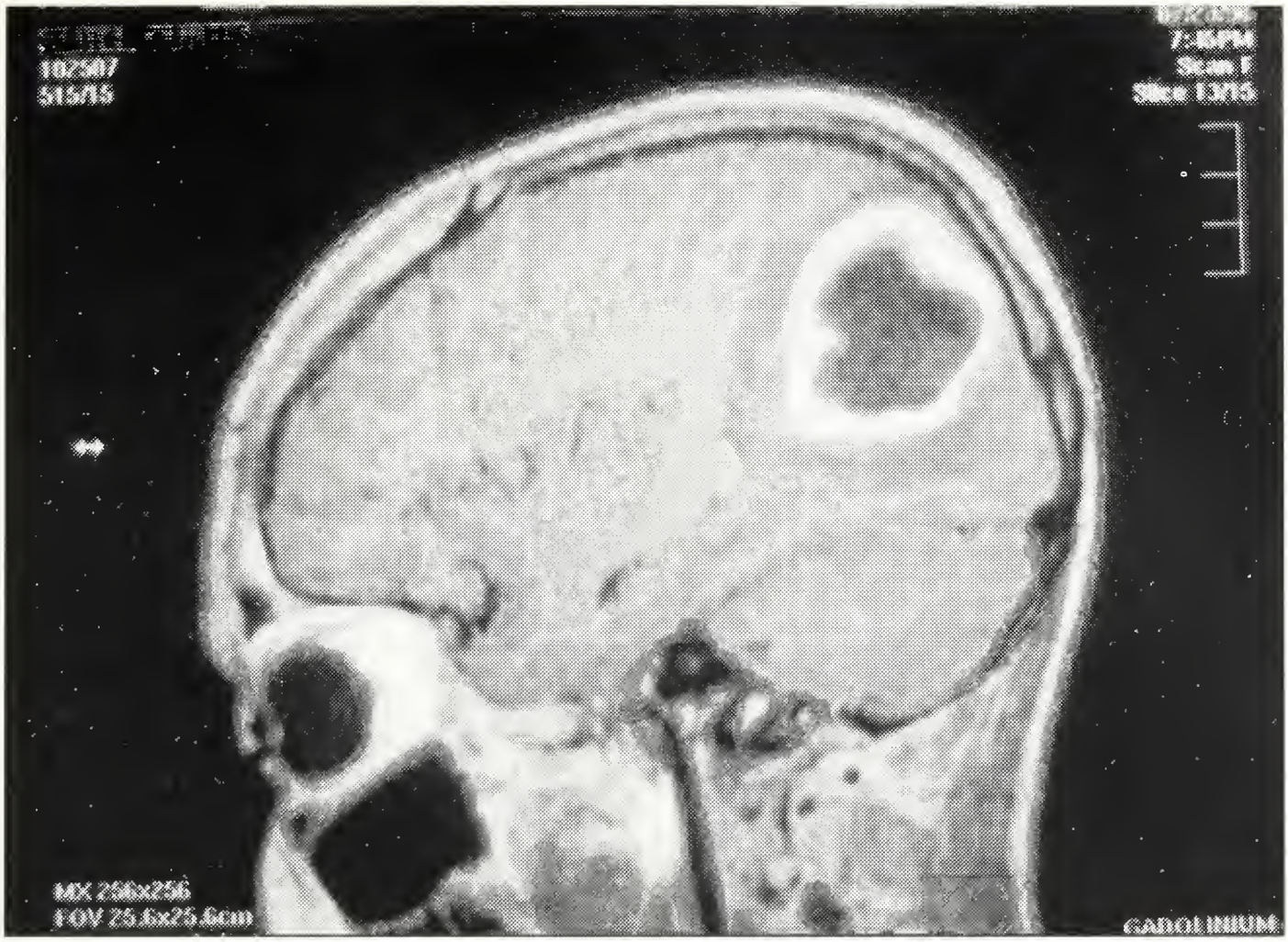


Figure 2. Saggital and Coronal and axial magnetic resonance image of the brain demonstrating a ring-enhancing lesion in the right posterior parietal / occipital region pre-operatively. continued on next page



continued - Figure 2. Saggital and Coronal and axial magnetic resonance image of the brain demonstrating a ring-enhancing lesion in the right posterior parietal / occipital region pre-operatively.

perceive persisting images, such as the face of a nurse, or on his television screen displaced into his left field and persisting for several seconds after the original image was no longer in his fixation. There was only one such persistent afterimage. He denied diplopia. There were no symptoms consistent with seizure activity. His acuity remained J1 o however he had a complete homonymous left field defect by confrontation. Optokinetic nystagmus was asymmetric. He was orthophoric with no oculomotor deficiency. Pupils were reactive without relative afferent defect. He had no media irregularities and no abnormality of Enhanced Bruckner Test. Each retina and optic nerve was normal, specifically without macular edema or optic nerve edema.

DISCUSSION

Palinopsia is a type of visual perseveration persistent or recurrent visual images after the exciting stimulus object has been removed. Such non-retinal afterimages are often quite vivid and indistinguishable from the real object. Palinopsia is a rare symptom, especially in children (2). They are usually associated with a homonymous hemifield defect and parieto-occipital pathology (3). Palinopsia is the more specific of the types of positive spontaneous visual phenomena (4) . PSVP were never associated with auditory or other sensory positive phenomena, except in patients with agitated delirium. Patients with photopsias, phosphenes, palinopsia, and visual hallucinations had similar lesions in MRI/CT, suggesting no anatomic area unique for these four phenomena, however right-sided lesion predominate in palinopsia (1). However, there was a significant difference in the severity of associated necrologic deficits between hemianopic patients with and without PSVP. Larger lesions destroying anteriorly located visual association areas precluded the development of PSVP, which may be related to release from inhibitory input of visual regions bordering the damaged area. Patients with the syn-

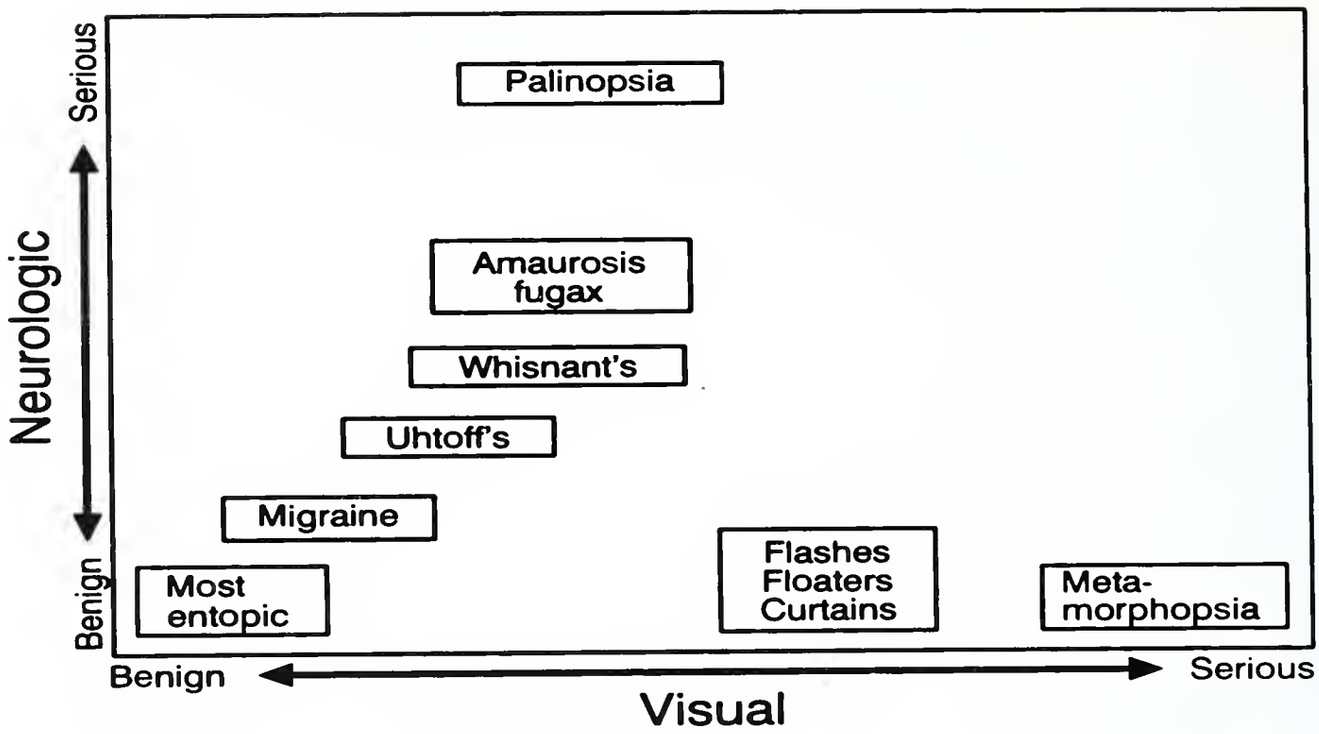


Figure 3. Diagram showing the relative seriousness of positive visual phenomena on the visual and neurological systems.

drome of agitated delirium and hemianopia had specific lesions involving the mesial aspect of the occipital lobe, the parahippocampal gyrus, and hippocampus.

Palinopsia must be distinguished from multiple other visual symptoms arising proximal to the environment (5). Metamorphopsia results from a distortion in the central retinal architecture such as a subretinal neovascular membrane or central serous chorioretinopathy. Polyopia can occur with distortions in the ocular media or from new-onset strabismus. Scintillating scotomata are associated with migraine; most are duc to CNS migraine with a binocular small gray expanding scotoma with fortification spectra at the periphery while a minority are retinal and monocular without headache due to proximal retinal vasospasm. Whisnant's sign is due to poorly perfused photoreceptors as a visual loss in bright light. Uhtoff's sign is a visual obscuration with exercise or heat associated with optic nerve inflammatory demyelination. Obscurations of the central vision often accompany pseudotumor cerbri and papilledema.

Entopic phenomena arc reproducible images which arise from structures within the eye itself. Most common, especially with myopia are "insect" or "cobweb" floaters or *muscae volitantes* with dark monocular images which move with a delay associate with an ocular saccade. Flashing light result from vitreous traction on the retina and frequently are associate with a retinal holes and detachment. Halos can be projected from the anterior refractile surfaces or the eye. 3 halos emanate from the corneal epithelium, 4.5 halos from the endothelium of the lens, 6 halos are from lens fibers and 7-12 displaced halos arise from keratopathy such as with acute angle closure glaucoma. Purkinje Figures are from shadows of the retinal vessels impinging on non-adapted photoreceptors. A similar mechanism causes "Luminous darting points" or "bluefield entopic phenomena" with white blood cells in the capillaries over the macula. It is possible to perceive "pulsatile retinal blood vessels" due to exercise or globe pressure in the parafoveal vasculature. Phosphenes, meaning "to show light" are colorful glows with alterations in the retinal or choroidal circulation due to globe pressure, rapid eye movement, accommodation and radiation. Blue arcs of the retina are secondary to electrical stimulation of the nerve fiber layer from a parafoveal source. Haidinger brushes occur 2.5 from fixation due to the macular xanthophyl response to polarized light. "Seeing Stars" after a blow to the head, Valsalva or quickly standing may result from tem-

porary tiny bubbles in the circulation.

Afterimages can be generated by the retinal response to bright light (6). Retinal afterimages correspond to the stimulus intensity, duration and size, they appear as a negative afterimage against a light background but a positive image against a dark background, they continue after a blink or eye occlusion, they appear in the central and peripheral fields. Retinal after-images are perceived by both eyes despite stimulus of only one eye. The images move with eye movement and the persistence correlates with electroretinogram activity. On the other hand, posterior geniculate after-images like palinopsia are not correlated with intensity, duration or color of the stimulus, they are not induced by prolonged fixation and they are not consistently induced. These higher cortical images my manifest as only parts of objects and appear as a positive object against a dark or a light background. Most images are stationary despite eye movement. Post-geniculate images occur with conscious, clearly mentating patients without anxiety. Most of these occur with structural abnormalities and occur within a relative field defect. Hallucinations are sensory impressions without an external stimulus and often are cinemascopic moving about in the visual field.

Some positive images are benign and some indicate serious disease with respect to ocular or cerebral structures (7) (Figure 3).

Noonan syndrome is a constellation of mild to moderate mental retardation, typical facies and posterior neck, high palate, low-set ears, shield chest, pulmonary stenosis with or without atrial septal defect and multiple pigmentary anomalies (8). There may be clubbing of the finger nails and hypertrophic cardiomyopathy. Noonan Syndrome occurs in about 1 per every 1000 liveborn infants and is primarily autosomal dominant. Bacterial brain abscess has rarely been reported with this condition (9).

Bacterial Brain abscess, especially in the absence of cardiac anomalies, is unusual (10). Streptococcus species have a predilection for the brain (11) and can cause a relatively rapid hemianopia (12). Magnetic resonance is particularly helpful in the diagnosis (13).

SUMMARY

Though positive visual symptoms can be psychological in nature, or can result from a perceptive or anxious patient recognizing optical principals in the eye itself, this case illustrates how a thorough history is required to delineate those rarer signs which accompany serious macular or neuro-ophthalmic pathology.

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ADH and *ALDH* Polymorphisms Among Alaska Natives Entering Treatment for Alcoholism*

Bernard Segal, Ph.D.[1]

ABSTRACT

The alcohol dehydrogenase (*ADHs*) and aldehyde dehydrogenases (*ALDHs*) involved in alcohol metabolism are polymorphic. Different alleles encode subunits of the enzymes that are related to differences in alcohol metabolism with different ethnic groups. This study examined the allele frequencies at the *ADH1*, *ADH2*, *ADH3* and *ALDH2* loci in Alaska Natives entering treatment for alcoholism to determine if allele frequencies at these loci differ among five distinct Alaska Native groups: Yupik and Inupiat Eskimos, Athabascan, Tlingit and Aleut. It was found that all persons were homozygous for the *ADH1*1*, *ADH2*1* and *ALDH2*1* alleles. Variations, however, were found for the allele distribution of the *ADH3* genotype. Comparison with a general population sample found no differences in allele distributions for *ADHs* and *ALDH2*1*, but differences were found when comparisons were made with four Asian Groups. The study's findings suggest that the Alaska Natives are not protected from the risk of alcoholism in the same way that Asians who possess the ALDH2*2 genotype are considered to have a negative risk factor. Nor, does there appear to be any generalized differences between Alaska Native alcoholics and members of the general population with respect to the *ALDH* and *ADH* polymorphisms studied herein.

INTRODUCTION

That polymorphism of alcohol-metabolizing genes affects drinking behavior and risk for alcoholism is well substantiated (Bosron & Li, 1986: Shen et al. 1997; Tanaka et al. 1997; Thomasson et al. 1991). The process of alcohol metabolism primarily occurs in the liver, and the rate of metabolism is governed by alcohol dehydrogenases (**ADH**s), which convert alcohol to acetaldehyde, and by aldehyde dehydrogenases (**ALDH**s), which convert acetaldehyde to acetate. Both **ADH**s and **ALDH**s are polymorphic. The **ADH**s involved in metabolism are homodimeric enzymes containing and subunits, encoded by *ADH1*, *ADH2* and *ADH3*, respectively. The *ADH2* and *ADH3* loci are polymorphic. *ADH2*1* encodes the $_{1}$ subunit, *ADH2*2* encodes the $_{2}$ subunit, and **ADH2*3** encodes the $_{3}$ subunit. **ADH** enzymes containing different subunits have different kinetic properties: $_{2}$ and $_{3}$ containing enzymes have a much higher Vmax than enzymes containing only $_{1}$ subunits. *ADH3*1* produces the $_{1}$ subunit, with a V_{max} higher that that of the $_{2}$ subunit encoded by the *ADH3*2* (Bosron & Li, 1986). Different alleles that encode subunits of the enzymes have been found to be related to different rates of alcohol metabolism within different ethnic groups (Li & Lockmuller, 1989; Segal & Duffy, 1992; Thomasson et al, 1991).

This study sought to further an understanding of the relationship between *ADHs* and *ALDHs*, examined the allele frequencies at the *ADH2*, *ADH3*, and *ALDH2* loci in Alaska Natives entering treatment for alcoholism. A specific aim of the research was to determine if differences were present at these loci among different Alaska Native populations.

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METHOD

Subjects

All subjects entering treatment were recruited from consecutive admissions to one of three inpatient alcoholism treatment facilities in Anchorage, Alaska. A total of 261 Alaska Native clients were interviewed as of fall, 1997, of whom 54% were male, and 46% female. The average age of the sample was 33.1 years (SD = 8.5), with an age range between 18 and 58 years. Of this total, 206 cases were genotyped, and this group constitutes the study population for this research.

The ethnic distribution was as follows: Aleut 23%; Yupik Eskimo, 19%; Tlingit Indian, 11%; Inupiat Eskimo, 17%; Athabascan Indian, 26%; Haida, 2%; Tsimshian, 1%; and mixed heritage, 1%. A Chi-Square test of the relationship between gender and ethnicity revealed no statistically significant differences (^{2} = 8.817, N = 261, df = 8, p = .358).

The comparison general population sample (N = 69) was obtained from residents (Yupik Eskimos) of Gamble on St. Lawrence Island, who completed a health questionnaire and provided blood samples as part of a larger study examining diet, coronary disease and diabetes among the island's residents.

Alcohol-Related Information

A complete and detailed lifetime drinking history was obtained from each subject using the Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA). The SSAGA interview schedule covers the major alcohol abuse and dependence criteria defined in DSM-III-R and DSM-IV, and has shown to have good reliability (Bucholz et al. 1994) and validity (Hesselbrock et al. 1997). Computer algorithms, developed for the Collaborative Study on the Genetics of Alcoholism (COGA) project were used to make all diagnoses.

Blood Samples

Blood samples in the three programs were drawn by a phlebotomist using appropriate sterile procedures. The non-fasting samples are appropriate for the types of blood studies undertaken. (Each 7 mL. vial was identified only by code number.) The vials were mailed within 24-hours to the Center for Alcohol Research, Indiana University Medical Center, for genotype analysis.

Blood samples were obtained from residents in Gamble by a qualified technician as part of a comprehensive physical examination. Blood drops on filter paper were provided for use in the present study, which were also forwarded to the Center for Alcohol Research and subsequently forwarded to Indiana for analysis.

Genotyping

Alcohol and aldehyde dehydrogenase genotyping was undertaken following the method established by Crabb et al. (1989) and Xu et al (1988).

RESULTS

Population Differences in Allele Frequencies

Allele and genotype frequencies were compared among the different Alaska Native groups comprised of individuals from the clinical population described above. It was found that the sample was essentially homozygous for possession of the ***ADH2*1*** and ***ALDH2*1*** alleles. The same results were found for the Gamble Island sample.

Table 1.

Genotypes and Allele *ADH3* Frequencies of Alaska Native Ethnic Groups Entering Treatment for Alcoholism

		ADH3				
		Genotype Frequency			Allele Frequency	
Ethnicity	n	*1/*1	*1/*2	*1/*1	*1	*2
Aleut	49	0.29	0.41	0.30	0.50	0.50
Yupik	41	0.15	0.56	0.29	0.43	0.57
Tlingit	24	0.29	0.33	0.38	0.46	0.54
Inupiat	30	0.37	0.60	0.03	0.67	0.33
Athabascan	52	0.17	0.52	0.31	0.43	0.57
Haida	2	0.00	1.00	0.00	-	-
Tsimshian	5	0.20	0.80	0.00	-	-
Mixed Native	3	0.00	0.67	0.33	-	-

Table 2.

Comparison of ***ADH3*** Genotypes and Allele Frequencies of Alaska Natives Entering Treatment for Alcoholism and a General Population Sample of Alaska Natives

		ADH3				
		Genotype Frequency			Allele Frequency*	
Ethnicity	n	*1/*1	*1/*2	*2/*2	*1	*2
Alaska Natives Entering Treatment	206	0.23	0.50	0.27	0.48	0.52
General Population	69	0.29	0.32	0.39	0.45	0.55

*In a previous study of 77 Alaska Native Alcoholics in Anchorage, the ***ADH3*1*** and ***ADH3*2*** allele frequencies were 0.45 and 0.55, respectively (Avksentyuk et al. 1994).

The occurrence of the **ADH3** genotypes and allele frequencies for the clinical sample is reported in Table 1, where a wide range of distributions is shown, but the variations were not statistically significant ($^2 = 25.494$ (df = 16), p = .061).

The data for the clinical sample were combined and compared with the Gamble Island sample, who were predominately Yupik Eskimo, in Table 2. The genotypes are about evenly distributed within the populations, and the differences between the two in ***ADH3*** allele frequencies were not statistically significant (F (1, 301) = 1.4300, p = 0.231). The allele distributions for both groups approximates a 50-50 distribution.

Table 3 presents a comparison of the ADH3 genotype distribution of the Alaska samples with ***ADH3*** data from four Asian Groups: Han and Elunchun Chinese, Koreans, and Monogolian (Shen et al. 1997). It is interesting to observe that not only do the ***ADH3*** genotypes appear to be distributed differently, but the allele frequencies tend to show a different distribution pattern among the four Asian populations when compared to the Alaska Native groups. The Alaska Native samples, as noted above, approximates a 50-50 allele distribution, while the four Asian groups tend to show, in many cases, about a 9:1 allele distribution.

It may also be noted that the Asian data disclosed differences in ***ADH2*** and ***ALDH2*** genotype and allele distributions among their study populations, whereas the Alaska populations were found to be homozygous at the ***ALDH2*** locus for the ***ALDH2*1*** allele, as well as homozygous at the ***ADH2*** loci for the ***ADH2*1/*1*** allele.

DISCUSSION

Consistent with previous findings (Avksentyuk et al. 1994, 1995 Segal & Duffy, 1992; Thomasson et al. 1992), little variation was found among the Alaskan Native samples regarding ***ADH1*1***, ***ADH2*1***, and ***ALDH2*1*** genotypes. The ***ADH3*1*** and ***ADH3*2*** alleles were evenly distributed within the population, with the *1/*2 genotype predominating. It thus appears that the allele distribution is not affecting the severity of alcoholism in this Alaska Native clinical population.

The genotype distribution, however, for the Alaska Native samples, tended to differ from those possessed by four different Asian populations. Alaska Natives tended to show greater variation in both ***ADH3*** genotype and allele frequencies, while being homozygous at the ***ALDH2*** and ***ADH2*** loci.

An implication of this finding is that Alaskan Natives *do not* resemble Orientals with respect to possessing a dominant **ALDH2*2** allele, and with respect to ***ADH3*** genotype and allele distribution. These results are consistent with the finding by Rex et al. (1985) that Native American Indians in Northern New Mexico were similar to White American and European populations, but different from those observed in Japanese and Chinese. The present

Table 3.

Comparison of ***ADH3*** Genotypes and Allele Frequencies of Alaska Natives Entering Treatment for Alcoholism and a General Population Sample of Alaska Natives with ***ADH3*** Genotype and Allele Frequencies from Asian Ethnic Groups*

		ADH3				
		Genotype Frequency			Allele Frequency	
Ethnicity	n	*1/*1	*1/*2	*2/*2	*1	*2
Alaska Natives Entering Treatment	206	0.23	0.50	0.27	0.49	0.51
General Population	69	0.29	0.32	0.39	0.45	0.55
Han						
Control	48	0.85	0.13	0.02	0.92	0.08
Alcoholic	52	0.81	0.15	0.04	0.88	0.12
Korean						
Control	50	0.90	0.10	0.00	0.95	0.05
Alcoholic	55	0.82	0.16	0.02	0.90	0.10
Mongolian						
Control	35	0.80	0.20	0.00	0.90	0.10
Alcoholic	31	0.65	0.32	0.03	0.81	0.19
Elunchun						
Control	37	0.73	0.27	0.00	0.86	0.14
Alcoholic	31	0.42	0.52	0.06	0.68	0.32

*Source: Chen et al. 1997.

findings also suggests that the Alaska Natives are not protected from the risk of alcoholism in the same way that Asians who possess the **ALDH2*2** genotype are considered to have a negative risk factor. Thus, there does not appear to be any generalized differences between Alaska Native alcoholics and members of the general population with respect to the ***ALDH*** and ***ADH*** polymorphisms studied herein.

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(continued on page 23)

STATUS OF GYNECOLOGIC HEALTH CARE IN THE CENTRAL ASIAN REPUBLIC OF UZBEKESTAN

By Doris K. Heilman, M.D.[2]

In November of 1998 I visited Uzbekestan with an Obstetrics and Gynecology needs assessment team for Northwest Medical Teams, Portland, Oregon. We were guests of the Tashkent State Medical University #1. We lectured to medical staff and students, visited facilities, and examined patients and scrubbed on surgery with their staff.

They follow the Moscow School of practice. Hospitalizations are much longer than in the United States and follow-up continues longer. Antibiotics and physiotherapy are the modalities of therapy for many problems.

They have almost no disposable supplies. Lap packs and surgical gloves are sterilized and reused. Suture is 3-0 silk, used single or double, and #3 chromic. Scalpels are dull and surgical instruments grip poorly.

In the face of these hardships their physicians are caring and brave. They are quite bright and they are keen to learn what we in the United States are doing.

Their program for treatment of pelvic inflammatory disease is particularly interesting. They have no tests for chlamydia. They treat with sulfa and intravenous antibiotics in the hospital. Physiotherapy follows, then low energy laser therapy. Finally hydrotubation is done about six weeks later. The objective is preservation of tubal patency. Fertility is very important in this predominantly Muslim country.

One of the professors M. K. Kattakhodjaeva asked us to submit her most recent paper on this subject for publication here. They do not have a system of private publishers, so it is not possible for them to reference their work using our system entirely. I have edited the paper to our format and to more proper English grammar than the original translation.

THE EFFECT OF LASER RADIATION ON THE METABOLIC PROCESSES OF CELLULAR MEMBRANES IN PELVIC INFLAMMATORY DISEASE

M.H. Kattakhodjaeva and L.SH. Rakhimova[1]
Edited by D.K. Heilman, M.D.[2]

ABSTRACT

The metabolic products of peroxide oxidation of cellular membrane lipids and the activity of the antioxidant enzyme superoxidismutase in blood plasma was determined in 68 patients with acute pelvic inflammatory disease and exacerbation of chronic pelvic inflammatory disease. The analyses were done before treatment, after routine antibiotic therapy, and after low energy laser radiation treatment. During acute inflammation and exacerbation of chronic inflammation, peroxide oxidation of cellular membrane lipids intensifies and antioxidant enzyme activity decreases. Helium-neon laser rays in addition to routine antibiotics appear to stabilize peroxide oxidation and normalize antioxidation enzyme activity more than antibiotics alone.

(1) Tashkent, Republic of Uzbekestan, First Tashkent State Medical University, Department of Gynecology and Obstetrics.
(2) Tanana Valley Medical and Surgical Group, 1001 Noble Street, Fairbanks, Alaska 99705. Send Requests for reprints to this address.

INTRODUCTION

More than half of all women visiting the Women's Polyclinic are suffering from pelvic inflammatory disease. About half of them are deemed in need of hospital treatment. Because of this, investigation of the pathogenesis and development of pathogenically valid methods of treatment are of great importance and urgency. The purpose of this study was to investigate the effect of laser therapy on the intensity of peroxide oxidation of cellular membrane lipids in patients with pelvic inflammatory disease.

METHODS

The intensity of peroxide oxidation of cellular membrane lipids [POL] and the activity of antioxidizing enzymes was studied in 68 patients. Their average age was 31.8 years (2,4). Fifteen healthy, nonpregnant women of childbearing age were used as controls.

The diagnosis of acute and chronic inflammation was made by complaints, history, clinical manifestations, ultrasound examination, and laboratory tests. Initial basic therapy consisted of antibiotics chosen according to the causitive organism and its sensitivity to antibiotics. Laser therapy was done using the helium-neon laser [GNR] at 25 mvt power and wavelength 638 nm. Depending on the severity and location of the disease, either endovascular laser radiation of the blood or intravaginal laser radiation of the vaginal vault and cervix was done in corresponding exposure and power.

The intensity of the POL process was determined by the level of toxic lipoperoxides of malone dialdehyse [MDA] in venous blood plasma and the intermediate metabolic product acilhydroperoxide [AHP]. In addition, the activity of the antioxidant enzyme superoxidismutase [SOD] was studied. These indicators were measured in three situations: [1] when the patient was admitted to the hospital, before treatment, [2] after the course of routine antibiotic therapy, and [3] after the course of laser therapy.

RESULTS

Twenty-two patients [32.4%] were having their first episode of pelvic inflammatory disease. Forty-six [67.6%] were having exacerbation of chronic pelvic inflammatory disease. 47% had inflammation located in the adenexa, 16% in the uterus, 10% had parametritis and pelvic peritonitis. On admission, 25% of the patients had severe disease, 43% had moderate disease, and 31.2 % had mild disease.

The chemical analyses show that, in acute inflammatory disease, peroxide oxidation of cellular

Table 1.

Groups examined	POL Products		Activity
	MDA [nm/ml]	AHP relative 1/ml	SOD%inhibition
Healthy women (control group)	3.69± 0.4	1.32± 0.1	72.4± 1.8
Patients with acute inflammation	8.92± 0.55 *	2.19± 0.28 *	49.6± 4.2 *
Patients who received basic therapy	8.05± 0.6 *	1.52± 0.2	64.5± 4.7 *
Patients who received laser therapy	5.4± 0.7 *	1.44± 0.3	73.2± 4.1

POL INTENSITY AND ACTIVITY OF ANTIOXIDANT ENZYMES

* reliable with respect to control group p <0.05

membrane lipids intensifies. This is demonstrated by the increase in toxic lipoperoxides of malone dialdehyse, 2.4 times that of the control group, and acilhydroperoxide, 1.7 times that of the control. The maximum MDA was 15.9 nm/ml, and the AHP was 2.56 relative 1/ml. [See Table 1.]

The results show that, in patients with acute inflammatory disease, superoxidismutase levels decreased from those of controls by a factor of 1.5. With basic antibiotic therapy, the SOD activity increased but was still lower than that in controls. Use of the low energy laser radiation raised the SOD activity level to correspond to healthy controls.

DISCUSSION

Previous studies have shown that peroxide oxidation of cellular membrane lipids forms free radicals by transfer of oxygen onto the substrate forming peroxides, aldehydes, and ketones. The peroxide compounds thus formed play a significant role in phagocytosis and lysis of microorganisms. However, excessive amounts of these products can be toxic, causing dystrophy of cellular membranes and promoting sclerotic changes in tissue and organs.

The system of antioxidation protection is of great importance for the maintenance of normal peroxide oxidation of cellular membrane lipids. One of the enzymes of the antioxidation systems is superoxidismutase. The increase in intensity of peroxide oxidation of cellular membrane lipids in pelvic inflammatory disease is likely promoted by the reduction of antioxidation enzyme activity.

This study demonstrated the sharp intensification of the process of peroxide oxidation of cellular membrane lipids and the decrease of antioxidant enzyme activity in acute pelvic inflammatory disease. Routine antibiotic therapy resulted in some reduction in the intensity of the peroxide oxidation process. However, the indicators of MDA and AHR remained higher than that of the control group. The use of low energy laser radiation to treat patients with pelvic inflammatory disease appeared to help stabilize the process of peroxide oxidation of cellular membrane lipids.

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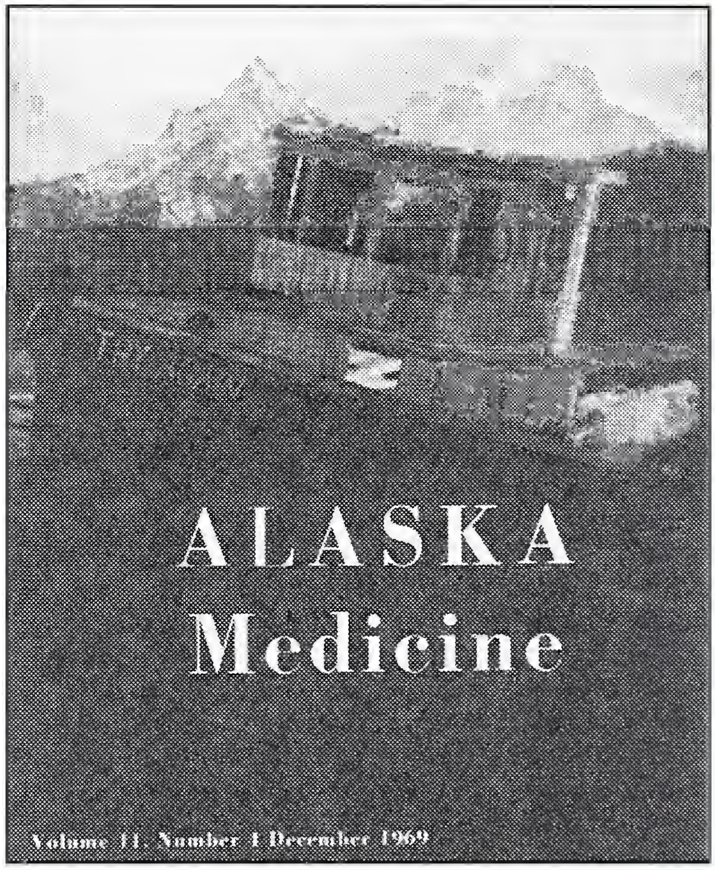
Correction

In the original article entitled "Regional Health Assessment relating to mercury content of fish caught in the Yukon-Kuskokwim Delta rivers system," published in Volume 40, No. 4, 1998 of *Alaska Medicine* should read micrograms per gram (g/g).

From Out of the Past — Over 30 Years Ago

Gloria K. Park, MD

Cover of Vol 11, No. 2 *Alaska Medicine*



Cover of Vol 11, No. 4 *Alaska Medicine*

ALASKA MEDICINE

Official Journal of the Alaska State Medical Association
Official Journal of the Alaska Dental Society

519 West Eighth Avenue, Anchorage, Alaska 99501

APPLICATION TO MAIL AT SECOND CLASS POSTAGE RATES IS PENDING AT ANCHORAGE ALASKA

Volume 11 June 1969 Number 2

TABLE OF CONTENTS

BUSINESS and ADVERTISING
Robert G Ogden *Executive Secretary*
519 West Eighth Avenue
Anchorage Alaska 99501

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The second quarter issue was printed June 1969 by Ken Wray's Print Shop Inc Anchorage*

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About the Cover
"Try Again" was photographed on Homer Spit one Arctic afternoon by Dr. Paul Eneboe (Nikomatic 105 mm. lens Kodachrome X at F 8.0 — 1/125 second)

Table of Contents, Vol 11, No. 4 *Alaska Medicine*

The following are obituaries that appeared in the 1969 issues of *Alaska Medicine.*

WILLIAM O. MADDOCK, M.D.

1923 - 1969

William O. Maddock was born in Tacoma, Washington, on November 25, 1923. He completed high school in Seattle and finished his premedical requirements, with honors, at the University of Washington. During these three years, he filled his leisure time as an orderly at King County Hospital.

Entering the University of Oregon School of Medicine in 1943, he soon began research in Endocrinology. This field remained his greatest academic interest. He graduated at the head of his class and received his Master of Science degree in June, 1947, and his Ph.D. and M.D. in 1948.

Although the youngest, he was considered the most capable member of his class.

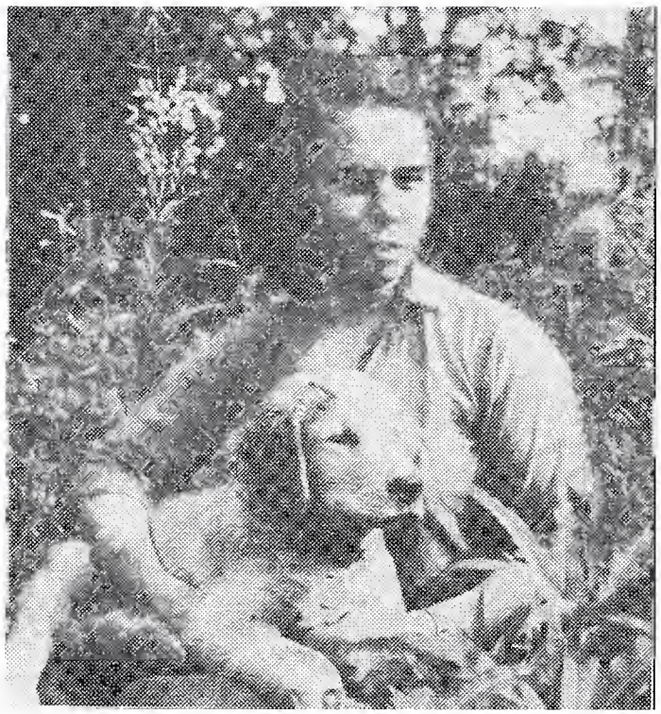
During the years at Portland, he married Alice, his life-long companion. They moved to Detroit in 1949, where he interned at the Detroit Receiving Hospital and then accepted a fellowship in Internal Medicine until 1952. He was also an Instructor at Wayne University School of Medicine, where he continued his research.

From October, 1954 until October, 1956, he served with the Army in Korea and in Japan and then returned to Detroit. He was appointed Associate Professor of Medicine at Wayne in 1956, and became a member of the American Board of Internal Medicine in 1957. He was also a member of the American Society for Clinical Investigation, the American Federation for Clinical Research, the American Physiological Society, the Endocrine Society, the Society for Experimental Biology and Medicine, and the Central Society for Clinical Research. In his field, he was broadly recognized.

In 1958, tired of organized medicine, he came to Alaska and started private practice in Anchorage. He served a term as Chief of Staff of Providence Hospital, the first editor of A*laska Medicine,* and Director of The Doctors' Clinic in Anchorage.

Bill Maddock was ever anxious for the happiness and welfare of mankind. He missed no opportunity to encourage his patients and colleagues. He died suddenly following an accident on January 5.

ROSALIE SHOHL, M.D.
1927-1969



Dr. Rosalie Shohl died at her home on Tanaina Drive in Anchorage on April 18, 1969, following a prolonged illness. Born in Columbia, South Carolina, she attended Duke College and the University of Pennsylvania Medical School, where she graduated A.O.A. in 1951. In Philadelphia Rosalie married Theodore Shohl, who had graduated from University of Pennsylvania Medical School and was at that time a resident in general surgery. After internship and a year of medical residency at Philadelphia General Hospital, Rosalie completed her anesthesiology residency at the Philadelphia General Hospital with Dr. Eugene Connor and Dr. Margo Deming. She then continued on in practice there until the birth of their first child, Barbara, in 1956.

The Shohls practiced in California for three years before moving to Alaska in 1960 with Barbara and Peter who was born in 1958. David and Margo were born in Anchorage in 1960 and 1962.

Rosalie had joined the League of Women Voters in California and was also active in that organization here in Anchorage, at one time serving on the board of directors.

Ted and Rosalie brought with them to Alaska an interest in recorders and recorder music and were responsible for starting the Anchorage recorder group.

Rosalie loved the out-of-doors and the family spent a lot of time hiking and camping together. She was an ardent bird-watcher and loved Alaska's wildflowers, interests which she has passed on to her children. The Campfire Girls were her favorite community project and she served as leader or assistant leader during the past five years. Rosalie worked hard to help establish the resident camp facilities for the Campfire Girls at Kenai Lake, and helped formulate the medical standards and procedures for the camping program as well.

Over the past several years Rosalie and Ted entertained a number of students from the Far East who had visited in the United States under the State Department's Experiment in International Living. These young people stopped in Anchorage on their way home and Rosalie arranged for their housing, taking her own group of students on sightseeing tours and camping expeditions during the five or six days they stayed in Anchorage.

One of Rosalie's favorite musical compositions, the Schubert Mass in G, was performed in her memory by her friends on Sunday, May 18, 1969 at Alaska Methodist University. Ted and a number of other Anchorage physicians were in their usual musical roles as the chorus and orchestra presented a moving tribute to her before a silent group of her friends.

Elaine Mills

MERRITT PAUL STARR, M.D.

1920-1969

Doctor Merritt Starr died in Houston in August, one month after open heart surgery. He had had three valves implanted by Doctor Denton Cooley. Merritt loved life and fought hard to survive his surgery—the odds were against him even living a month postoperatively. While critically ill and awaiting surgery, Merritt realized one of his most sought after goals—he was awarded a $100,000.00 grant by N.I.H. to administer a cancer research project in California which he had proposed, involving the use of radioactive Boron in the therapy of cancer. He is one of few physicians in private practice to be honored by such a grant, and undoubtedly the only one in Alaska.

Merritt came by his interest in medicine, teaching, and research naturally. He was born in Winnetka, Illinois, the son of Doctor Paul Starr who was then a clinical professor at Northwestern University Medical School and now a clinical professor at Stanford. He attended Oberlin College in Wisconsin and was a Nu Sigma Nu at Northwestern Medical School. He took his internship and residency at King County Hospital in Seattle. Interns he supervised there included Vernon Cates and Bill Ivy, and his chief floor nurse on the medical service was Grace Cates. One of his students in the student nursing program was Gerrie Ivy who remembers him as a spellbinding and inspiring lecturer, even tho sometimes tardy and covered with blood or fish scales.

Alaska intrigued Merritt and he spent the summers of 1948 and 1949 working as a cannery physician. He made Alaska his permanent residence in 1950, opening his practice in internal medicine, associated with his former students Vern Cates and Bill Ivy. This association led to his becoming one of the founders of the Doctors Clinic (now the Alaska Clinic in Anchorage) where he supervised the development of the internal medicine department.

Dr. Merritt Starr had an insatiable curiosity to find the cause of any and every disease. He went to Seward many weekends to fish, but more often on those trips he became involved in discussion of newer treatments of tuberculosis, then the scourge of Alaska. His long time friend, F. J. Phillips, was then in charge of the Seward Sanatorium, where 150 patients with active tuberculosis of some form were hospitalized. Their association resulted in important health contributions to Alaska. Dr. Starr and Dr. Phillips, with the assistance of Dr. Wilkins. reactivated a chest clinic at the Greater Anchorage Health District for outpatient treatment of tuberculosis. Along with this, new advances were made in the treatment program at the Seward Sanatorium where Doctor Starr was Chief Medical Consultant.

H e approached any disease treatment problem with the thought "let's treat the cause of sickness as well as the sickness itself". He devoted much time to art, music, science and literature as well as world affairs and politics. He enjoyed hunting and fishing and was an enthusiastic boat builder.

Doctor Starr knew he was a handicapped person. He knew his heart would fail him sooner than later, yet he kept working to his physical limits at research ideas and clinical practice.

He must be remembered as a courageous and vigorous man with great integrity and loyalty. He was selflessly motivated by compassion for the infirm and for the poor. He did as much as possible for humanity in his forty-eight years.

1969
ALASKA STATE MEDICAL ASSOCIATION NEWS

By Robert Ogden

Representatives of Alaska State Medical Association's Legislative, Professional Insurance and Medico-Legal Committees traveled to Juneau March 26th at their own expense to testify on several bills before the Legislature. Physicians testifying were: James Lundquist, M.D., President, ASMA; Paul Isaak, M.D., President Elect, ASMA; Stan Jones, M.D., Vice President, ASMA; Rodman Wilson, M.D., Chairman, Legislative Committee, ASMA; Ed Spencer, M.D., Southeastern Councilor, ASMA; Bob Schuler, M.D., Past president, ASMA; Arndt van Hippel, M . D ., Chairman, Medical-Legal Committee, ASMA; Fred Hood, M.D., Anchorage; Gary Hedges, M.D., Juneau; Bob Smalley, M.D., Juneau.

Bills that A.S.M.A. members testified on were as follows:

S.B. 148: A bill regarding malpractice actions in the state. Senator Elton Engstrom of Juneau introduced a bill whereby malpractice actions based on the negligence of a physician or dentist would be brought against the state. The A.S.M.A. endorsed the principle of the bill, but realizing that it would be difficult to pass this type of legislation, passed on a number of alternate suggestions to the Judiciary Committee of the Senate including elimination or restriction of attorney contingency fees, establishment of a medico-legal review panel, pre-trial arbitration, a shortened statute of limitations, etc. The Judiciary Committee agreed that some type of legislation was needed to control the "capriciousness" of professional insurance availability and premiums. They indicated they would assist the Alaska State Medical Association in writing and passing legislation.

H.B. 326: Regarding Medical Licensure. This bill passed the Legislature April 19, 1969 and will go into effect immediately after the Governor's signature. This bill provides the following additions and deletions from our current statutes:

1. Will give the Alaska Board of Medical Examiners the power to use the Federal Licensing Examination (FLEX). This examination is written by the Federation of States Medical Boards of the United States, Inc. The basic objectives of the FLEX examination are as follows:
   A. To provide State Medical Boards with high quality, uniform, and valid examinations for purposes of evaluating clinical competence and qualification for licensure.
   B. To place licensure in a definite relation to modern medical education by updating state board examination procedures and providing flexibility.
   C. To establish uniform levels of examination between these states.
   D. To create a rational basis for interstate endorsement.
2. Repeals the Basic Science requirement for physicians in Alaska.
3. Repeals the citizenship requirements.
4. Adds a 90 day temporary permit for Locum Tenens who wish to assist Alaskan physicians.

C.S.S.B. 8: Regarding Air Pollution in the State. C.S.S.B. 8 passed the Legislature and was recently signed by the Governor. The bill provides for regulations to "achieve and maintain levels of air quality that will protect human health and safety, prevent injury to plant, or animal life, and promote the economic and social development of the State and facilitate the enjoyment of the natural attractions of the State. " A.S.M.A. members testified for the Air Pollution Bill and encouraged its passage.

H.B. 312: Regarding Therapeutic Abortions. This was discussed with the House Committee on Health and Welfare but an official A.S.M.A. position was not presented pending a poll of the membership.

C.S.S.B. 23: Regarding determination of permissible breath, urine, or blood alcohol levels when driving a motor vehicle. The A.S.M.A.'s Legislative Committee requested the introduction of this bill and assisted Senator Lowell Thomas, Jr. in the fight for passage. The bill passed and has been signed by the Govemor.

The A.S.M.A. position on medicaid was presented in February by the Legislative Committee as follows:

OLD AGE AND SURVIVORS INSURANCE ACT, TITLE XIX (MEDICAID) — The Alaska State Medical Association favors the adoption by the State of Alaska of Title XIX. This legislation providing financial medicaid assistance would significantly expand the present welfare program and make a wider variety of health services available to a larger number of citizens. On the basis of the Ernst and Ernst study it appears feasible, if not advantageous, for the State of Alaska to proceed with Title XIX, at the B level (annual income of $3,000 or less for a family of four). Continuance of the existing program is projected to cost the State 8.2 million dollars in 1970 and 13.5 million in 1975. With Title XIX, the 1970 cost would be 7.8 million, a savings of almost one half million dollars. In 1975 with Title XIX, Alaska would have a 19 million dollar program at a cost of 14 million dollars, very slightly more than continuing the present program.

From the Editor . . .

ALASKA MEDICINE, INTO THE MILLENNIUM

As we stand at the End of the Millennium, *Alaska Medicine* faces a set of challenges that have been increasing and are reaching near crisis proportions. We have good news to add as well, however, as we turn the calendar to the fabled year 2000. We have the core group of Editorial Board members who are giving generously of their time and energy to provide you readers and members the finest of an increasingly reduced number of state medical journals. Ours is truly the last of the scientific publications sponsored by a state association. We should be proud to carry our tradition of science and academic achievement especially in the areas of arctic research and northern latitude studies to all the world.

We welcome Dr. Robert Arnold to the Board and seek other new members to help broaden our scope of medical expertise and provide new insights. We will continue to depoliticalize this publication and act as the rallying flag for our organization and our state's medical profession. We are happily increasing the number of new members in our state and look forward to their contributions.

We do face, however, the very real and increasing threats to our continued existence. These are the same demons which have forced the closure and change of venue of our sister state medical journals. The twin dragons are lack of support by authors who have in the past year presented us with only 14 total articles for review. This makes for limited options for us as an editorial committee to continue to sustain our hard won depth and breath of medical coverage. With our close ties via academia with the University of Washington, our own residency and CDC Branch we should be producing more rather than less in both quality and quantity to carry to the world at large!

We face, as well, a fiscal threat as our costs continue to rise and we need to remain solvent within our organization as we come to request our annual funding. We have made several decisions as a board to help remedy these vital concerns. We plan to reduce the number of issues starting in 2000 to three per year and thereby reduce the pressure for new increases in subscription rates.

We can hopefully be increasingly more selective in our articles and will provide new features to broaden our appeal to all practitioners. We will push ahead to appeal for better and more generous sponsors to defray our overhead as well.

Please continue to give us your thoughts and medical expertise in articles, original and review, and we can carry a great tradition into the 21st Century.

Thank You

(continued from pg 12 - ADH and ALDH Polymorphisms)

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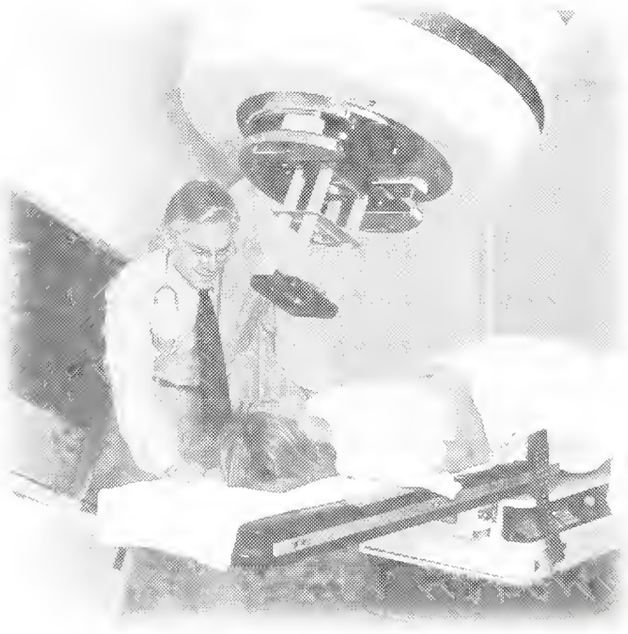

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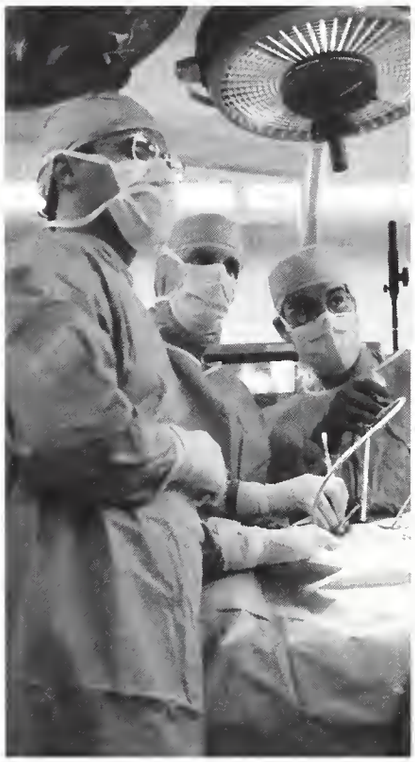

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Bacterial pathogens in chronic otitis media with effusion in Alaska Native children

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ABSTRACT

This study examined the bacterial pathogens and the presence of possible risk factors for the development of chronic otitis media with effusion (OME) in a group of Alaska Native children. Middle ear aspirates were collected from 128 children <6 years of age requiring tympanocentesis between 1987 and 1989. Bacterial pathogens were cultured from 40% of 209 fluids. Predominant isolates, after contamination of the outer ear was controlled for, were *Haemophilus influenzae* (21%; 84% of these were nontypeable), *Streptococcus pneumoniae* (8.1%; serotypes 6B, 10A, 11A, 14, 18B, 18C, 19A, and 23F), *Staphylococcus epidermidis* (3.8%), and *Moraxella (Brahmanella) catarrhalis* (2.9%). Pneumococcal-C-polysaccharide (PnC) was detectable in 3 of 135(2.2%) aspirates that did not grow *Streptococcus pneumoniae.* Combining culture and PnC assay results evidence of pneumococcal infection was found in almost 10% of aspirates tested. There was not a significant difference in the number of episodes of acute otitis media after the first year of life based on the age at the first episode (<6 mo, ≥6 mo). However, 88% of infants in the study had their first acute otitis media episode before 1 year of age.

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INTRODUCTION

Otitis media and its complications have historically been a major cause of morbidity not only among the Alaska Native but also among children of other North American Indian populations. Several studies conducted in the 1950s and 1960s in Alaska reported acute otitis media (AOM) as the second most common cause of morbidity among Alaska Natives (1,2). In a 1982 survey of four villages, chronic otitis media with effusion (OME) occurred in 8.9% of persons under 20 years of age and 21% of children under 5 years of age (3). The persistent effusion following AOM was once thought to be sterile. Yet in recent years, it has been firmly established that one-third to two-thirds of effusions contain pathogens (4,5). In Alaska, as in other parts of the United States otitis media is the most common cause of health care visits, contributing to a significant economic burden on the health care system (6). The prolonged duration of middle ear effusion in the first 3 years of life may be associated with lower cognitive ability, impaired development of speech and language and poor school performances (7,8). Despite the historical impact of otitis media in Alaska, there have been no systematic studies to determine the bacterial etiology of OME in Alaska Native children.

MATERIAL AND METHODS

Study population.

The 128 study participants resided in the Yukon Kuskokwim Delta (YKD) region and who had been scheduled for tympanotomy tube insertion for treatment of chronic OME (Table 1). Forty-three of the patients (33.6%) were from Bethel which comprises approximately 17% of the YKD population, and 85 (66.4%) were from surrounding small villages of 100-700 residents each. Village children are usually seen for routine and acute care in the villages by

Table 1.
Age and sex distribution of Alaska Native children with otitis media with effusion undergoing tympanotomy

Age (Years) at Tympanotomy	Male N (%)	Female N (%)	Total N(%)
0	5(3.9)	2(1.6)	7(5.5)
1	25(19.5)	25(19.5)	50(39.1)
2	15(11.7)	9(7.0)	24(18.7)
3	14(10.9)	10(7.8)	24(18.7)
4	5(3.9)	5(3.9)	10(7.8)
5	6(4.7)	7(5 5)	13(10.2)
Total	70(54.7)	58(45.3)	128(100)

community health aides who can dispense antibiotics under physician's orders. The children from Bethel are routinely cared for by a physician. At the time of the study, participants were from 8 to 70 months of age (median 25 months).

Sample collection and microbiology.

Tympanocentesis and tympanotomy were performed at the YKD regional hospital in Bethel on seven occasions over 2 years, from August 1987 to August 1989. Middle ear aspirates (MEAs) were collected aseptically using a sterile disposable trap under general anesthesia. Prior to incision, the tympanic membrane was sterilized with Betadine Surgical Scrub for 60 seconds, washed with sterile saline, and cultured to document outer ear microbial contaminants. MEAs with any outer ear bacterial contamination were not included in the analysis. MEAs were cultured aerobically on blood and chocolate agar in the presence of 5% CO_2. Bacterial isolates were identified and serotyped by using standard methods. Antimicrobial susceptibilities were performed by agar dilutions (9). MEAs were tested for pneumococcal-C-polysaccharide by enzyme immunoassay as previously described (10).

Data collection and analysis.

At the time of tympanotomy, each patient's hospital chart was reviewed. All episodes of otitis media were recorded, as were demographics such as age, sex, and village of residence. Eight children had incomplete charts. Statistical analysis was performed by using the Wilcoxon non-parametric rank sum test. A chi-square test or Mantel-Hanszel test was done on dichotomous data. All p values are two sided, and $p<0.05$ was considered statistically significant (11).

A recorded diagnosis of otitis media was taken as evidence of an episode of acute otitis media (AOM). Age at first onset was defined as the age at which the diagnosis of AOM was first recorded in the chart. The laterality of each infection was noted and coded as either left, right, both, or unspecified. When a unilateral otitis media was followed by inflammation in the opposite ear or inflammation that affected both ears, it was considered a new episode. If a unilateral otitis media was followed by an unspecified otitis media, it was considered to be the same infection. Since many of these children had frequent, recurrent bouts of otitis media and were seen numerous times for each infection, 21 days was arbitrarily selected as the cutoff that defined one episode from another. If a patient had a visit with a recorded diagnosis of otitis media within 21 days of a previous visit with a diagnosis of otitis media, the two were counted as the same episode. This resulted in some children with persistent episodes lasting over 100 days. To adjust for severity or persistence of infection in the analysis, any episode lasting 22 to 42 days was counted as two episodes and any episode lasting 43-63 days was counted as three episodes. Episodes per year of life were established based on this formula and calculated through the age of the child at the time of the MEA.

RESULTS

Bacterial etiology of otitis media with effusion.

Of the 226 MEAs recovered from 128 patients, 17 were excluded because of contamination of the outer ear. Eighty-four of the 209 (40.2%) had positive cultures (Table 2). *Haemophilus influenzae* (44 isolates; 21.1%) and *Streptococcus pneumoniae* (17 isolates; 8.1%) were the predominant pathogens. Eight (3.8%) grew *Staphylococcus epidermidis; six* aspirates (2.9%) grew *Moraxella (Brahamanella) catarrhalis* and two (1.0%) grew alpha streptococcus. Seven aspirates (3.3%) grew other organisms, including Group A *Streptococcus* (1), *Enterococcus faecalis* (1), *Enterobacter cloacae* (1), *Staphylococcus aureus* (1), Group D *Streptococcus* (1), and *Micrococcus sp.* (2). Of 44 isolates of *Haemophilus influenzae* 37 (84.1%) were non-typeable and 5 (11.4%) were type b; the remaining two were type a and type c. Fourteen of 44 (31.8%) of *Haemophilus*

Table 2.
Bacterial pathogens isolated from middle ear aspirates (n=209) from Alaska Native Children with otitis media with effusion.

Isolate	Number(%)
Haemophilus influenzae	44(21)
Streptococcus pneumoniae	17(8.1)
Moraxella (Brahamella) catarrhalis	6(3.9)
Staphylococcus epidermidis	8(3.1)
Streptococcus viridans	2(1.0)
other*	7(3.3)
Total isolates	84(40.2)

*Group A *Streptococcus, Enteroococcus faecalis, Enterobacter cloacae, Staphylococcus aureus,* Group D *Streptococcus,* Micrococcus species.

influenzae strains were beta-lactamase positive; two of these were type b, and 12 were non-typeable.

Eight pneumococcal serotypes were recovered: 23F (4), 19A (2), 18B (2) 18C (2) 11A (2), 14 (2), 10A (1), 6B (1). One isolate was not serotyped. Of the 17 pneumococcal isolates recovered, 4 (23.5%) demonstrated intermediate resistance to penicillin (MIC 0.1-1.0 g/ml), but were fully susceptible to all other antibiotics tested. Of these, 2 were serotype18C, 1 was 6B, and one was not serotyped.

Of the 226 MEAs, 203 were tested for pneumococcal-C-polysaccharide (PnC) by enzyme immunoassay. PnC was detected in 11 of 16 samples that grew *Streptococcus pneumoniae.* Of 125 sterile samples, one was PnC positive. One of four samples that grew *Haemophilus influenzae* type b, and one of six samples that grew *Staphylococcus epidermidis* were PnC positive.

Antecedent otitis media episodes.

Otitis media histories were obtained from 120 children. Sixty-five (54.2%) had their first episode before the age of 6 months; 41 (34.2%) had their first episode between the ages of 6 and 11 months; 9 (7.5%) had their first between 12 and 17 months; 3 (2.5%) between 18 and 23 months; and 2 (1.7%) were between the ages of 24 and 29 months (Table 3). The median age at first episode was 5 months (range <1 to 29 months). The median age at first episode was signficantly younger for Bethel children (3 months) than for village children (6 months) (p.=0.009).

There were no significant differences by gender in the number of episodes experienced by each child. However, there were differences by residence. The range of the average number of episodes per year for Bethel was <1 to 9 with a median of 4 episodes per year, whereas for village children the range was also <1 to 9 but with a median of 2 episodes per year (p <0.001). After adjustment for age at MEA, there was no difference between the number of episodes experienced after the first year of life by those with an age of onset <6 months compared to those with an age of onset of ≥6 months (p=0.44 for Bethel children, and p=0.21 for village children).

DISCUSSION

We found that the bacterial causes of chronic OME in this study were consistent with those found in other populations (4,5). Almost 40% of MEAs yielded bacterial isolates; with the predominant pathogens being *Haemophilus influenzae* and *Streptococcus pneumoniae.* Of the *Haemophilus influenzae* isolates, one-third were beta-lactamase positive (ampicillin resistant). These rates of antibiotic resistance are comparable to other studies in other areas (4,12). Among type b *Haemophilus influenzae* isolates recovered from Alaska Native children with invasive disease between 1987 and 1989, 45% were resistant to ampicillin (unpublished results). Rates of intermediate penicillin resistance among MEA pneumococcal isolates were higher (23.5%) than rates (17%) found among invasive pneumococcal isolates recovered from other normally sterile sites in Alaska Natives residing in the YKD during the same time period (13). However, this was less than the rate of 29% non-susceptible to penicillin (all intermediate) found among nasopharyngeal pneumococcal isolates recovered from children < 5 years of age in the YKD during 1992 (14). The pneumococcal serotypes found in the MEAs of our patients were again similar to those recovered from children in the same region with invasive disease and to those found in other pediatric studies (13,15). Most of these types are emerging as those most commonly non-susceptible to penicillin, either alone or in combination with resistance to erythromycin, trimethoprim sulfamethoxazole, and extended spectrum cephalosporins. Many of these serotypes have been established as etiologic agents in recent outbreaks of multi-drug resistant otitis

Table 3.
Age at first episode of otitis media in Alaska Native children with otitis media with effusion.

Age (Months) at first episode	Male N(%)	Female N(%)	Total N(%)
0-5	36(54.5)	29(53.7)	65(54.2)
6-11	21(31.8)	20(37.0)	41(34.2)
12 or more	9(13.6)	5(9.3)	14(11.7)
Total	66(55.0)	54(45.0)	120(100)

media and invasive pneumococcal disease elsewhere (16,17).

Of additional interest in our study was the presence of PnC in 2 of 67 (3.0%) of cultures that grew organisms other than *Streptococcus pneumoniae* and in 1 of 125 (0.8%) of MEAs that were sterile. After combining culture and PnC enzyme immunoassay results, evidence of pneumococcal infection was found in almost 10% of aspirates tested, suggesting that *Streptococcus pneumoniae* may be responsible for a larger fraction of OME than can be determined by culture alone. Detection of PnC may be of particular importance due to the accumulating evidence of the role of pneumococcal cell wall components in the inflammatory process in experimental otitis media (18,19). It has been hypothesized that cell wall components are a persistent remnant of prior pneumococcal infections in otherwise sterile OME. Although we found evidence of PnC in only 2% of MEAs not yielding *Streptococcus pneumoniae* by culture, in one other study about one-third of culture-negative acute effusions contained PnC (20), and higher levels of antibody to PnC have been demonstrated in middle ear effusions of children with OME (21). In addition, there is experimental evidence that penicillin accelerates the release of cell wall debris in the middle ear and cerebrospinal fluids (22,23). The detection of PnC in MEAs of these chronic OME patients in our study suggests a potential pathogenic mechanism for continuing inflammation in the absence of viable bacteria.

Risk factors for recurrent and severe otitis media include age at first episode, sex, season, familial aggregation, lack of breast-feeding, day-care attendance, and tobacco smoke (24). Of these, age at the initial episode of AOM is most significantly associated with recurrent AOM, which may lead to OME (24,25). Marchant et al. (26) found, in their prospective study of infants who had onset of otitis media before 2 months of age, that these infants had a 33% chance of developing otitis media with effusion for 3 months or longer. This risk was eight times that experienced by the remainder of the study population. The early onset group comprised fully 80% of those in their study who developed OME with effusion. In Australian Aboriginal infants, early onset of AOM correlates with early and rapid colonization of the nasopharynx with *Haemophilus influenzae* and *Streptococcus pneumoniae* (27). In this population early colonization may be attributed to high rates of cross-infection caused by overcrowded living conditions, poor hygiene and high rates of bacterial carriage. While our study population consisted only of those children with OME requiring tympanocentesis, in a retrospective record review, we found no difference between the number of acute episodes experienced after the first year of life in those <6 months of age at first onset, compared to those ≥6 months at first onset. However, a total of 88.3% of the study population had had their first AOM episode before the age of 1 year. This is consistent with other studies conducted with Alaska Native children, many of whom have their initial attack before the age of 1 year (28,29). Some studies consider <2 years to be "early", in which case 97.4% of our cases would have had an early age of onset (30). But the majority of AOM among children in the United States occurs between 6 and 18 months. In a prospective cohort study of children in Boston 25% had had at least one episode of AOM by 6 months of age, and by one year 62% had had at least one episode (31). However, within our study it is difficult to assess the risk associated with this early age of onset because of the lack of a comparison group of children who did not require tympanocentesis and did not have early otitis media. It has been suggested that for OME, it is not the early age of onset that is the risk factor but rather the recurrent number of episodes. Takasaka (32) found in their Japanese study that the risk for OME increases fivefold in children with acute suppurative otitis media. Other studies have confirmed that the risk of OME correlated with the number of recurrent episodes (33-35). Todd (36) in his study of otitis media in four populations in Arizona, found that 17% of "high risk" children, defined as having two separate clinical encounters of otitis media before 2 years of age, developed chronic OME. In contrast, of children having none or only

one clinical encounter in the first 2 years of life, only 3.3% developed chronic OME. Likewise our findings reflect that children who were <3 years of age at the time of MEA experienced more episodes of AOM in their first year of life compared to those who were ≥3 years of age at the time of MEA (p=0.010). It may be that these children have an inability to clear middle ear fluid, rendering them more susceptible to recurrent AOM and the development of persistent effusions at an earlier age. However, again, the lack of a comparison group of children not requiring tympanocentesis restricts conclusions.

Some studies suggest that males have more frequent attacks of AOM and are affected at an earlier age than females (31,34). Other studies, however, have suggested that gender differences only applied to the risk of AOM and that the risk factors for chronic otitis media with effusion may be different than those for OME, since as both sexes seem equally affected (35-37). Studies in Alaska appear consistent with these latter reports (29).

Although antibiotics are no longer recommended for the initial treatment of OME, the frequent recovery of drug resistant bacteria from MEAs has implications for the treatment of AOM (38-40). It is likely that these organisms will continue to play a predominant role in treatment failures of AOM and in chronic OME. There remains, however, a strong likelihood that some of the morbidity from otitis media will be preventable. Current success with the widespread use of conjugate *Haemophilus influenzae* type b vaccine has reduced invasive disease due to *Haemophilus influenzae* type b in many regions of the United States including Alaska (41). In the YKD region of Alaska, an active passive immunization strategy was used to reduce the rate of invasive *Haemophilus influenzae* type b disease in infants <1 year of age, from 2960 cases/100,000 before 1989, to 302 cases/100,000 by the end of 1992 (42). The conjugate vaccine has been shown to reduce carriage of *Haemophilus influencae* type b in vaccinated children, but not in this population (43,44) and consequent reduction of this pathogen as a cause of otitis media should follow. However, only a very small proportion of otitis media is caused by *Haemophilus influenza* type b (2.5% in this study). A conjugate vaccine which may provide protection against otitis media caused by seven common pediatric invasive disease serotypes (4, 6B, 9V, 14, 18C, 19F, 23F) of *Streptococcus pneumoniae* has been developed and has been found to be both immunogenic, and efficacious, against invasive pneumococcal disease in infants < 2 years of age, is anticipated to be licensed within the next year (45). With the concomitant reduction in carriage of vaccine serotypes, this multivalent conjugate pneumococcal vaccine may be effective in preventing AOM caused by serotypes in this vaccine (46). Work is also progressing on protein based vaccines against non-typeable *Haemophilus influenzae;* these have been shown to be effective at preventing experimental otitis media in animal models (47-49). Consequently, vaccines directed at the prevention of the two most common pathogens causing acute otitis media may be important for this high-risk population of Alaska Native children. This may decrease the incidence of AOM in the first year of life, likely reducing subsequent recurrent disease. Followup studies of bacterial pathogens on OME in this population after the introduction of the conjugate *Haemophilus influenzae* type b vaccine and prior to the introduction of conjugate pneumococcal vaccines to determine the distribution of bacterial pathogens and antimicrobial susceptibility patterns appears justified.

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Special Feature from the CDC . . .

Emerging Infectious Diseases in Alaska and the Arctic: A Review and a Strategy for the 21st Century

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ABSTRACT

Emergence of new, previously unknown, and drug-resistant infectious diseases pose a major threat to global health. The emergence of infectious diseases in Alaska and the Arctic parallels the resurgence of infectious diseases worldwide. The Centers for Disease Control and Prevention has developed a strategy to revitalize the capacity to protect the public from emerging infectious diseases by improving four major public health activities: surveillance and response, applied research, infrastructure and training, and prevention and control. The plan targets high-priority emerging infectious disease problems and particular groups of people at increased risk. These target areas encompass a number of diseases of special concern in Alaska, such as drug-resistant *Streptococcus pneumoniae* infections, foodborne botulism, alveolar hydatid disease, viral hepatitis, *Helicobacter pylori* infections, *Haemophilus influenzae* type b bacteremia and meningitis, and infections of immunocompromised persons, pregnant women and newborns, and tourists. To address these and other emerging infectious disease issues, including the threat of bioterrorism in Alaska and the Arctic, future issues of *Alaska Medicine* will include updates on specific emerging infectious diseases for health care providers, clinical laboratory workers, and community public health professionals who form the front lines for recognizing, treating, and preventing emerging infectious diseases.

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Infectious Diseases in the 20th Century: Conquests and Complacency

At the beginning of the 20th century, infectious diseases ravaged Alaska. The "Great Sickness" of 1900, thought to be caused by concurrent epidemics of influenza and measles, killed up to one-third of the Native peoples of western Alaska (1). During the 1930s, the annual tuberculosis death rate among Alaska Natives (655/100,000 persons) was the highest known (2). As recently as 1950, infectious diseases were the leading cause of death in Alaska (3). However, the development of antimicrobial drugs made tuberculosis, pneumonia, and other life threatening infections seem conquerable. Vaccines dramatically reduced the incidence of diseases

of childhood such as diphtheria, whooping cough, and measles. Between 1960 and 1980, infant morality among Natives in southwestern Alaska fell five-fold, and much of this reduction was due to prevention of deaths caused by infectious diseases (4). Throughout the United States, life expectancy increased and mortality rates decreased drastically during the first half of the century, mostly due to decreases in infectious disease mortality (5). These gains led to the conviction among clinicians, public health professionals, and national leaders that infectious diseases would soon become a thing of the past.

However, even as great progress in treatment and prevention of infectious diseases fueled optimism throughout North America, penicillin-resistant strains of *Staphylococcus aureus* emerged as early as the 1950s, and global pandemics of influenza occurred in 1957 and 1968. The 1970s witnessed the emergence of a number of previously unknown infectious diseases including Legionnaires' disease, Lyme disease, toxic shock syndrome, and Ebola hemorrhagic fever. Even as acquired immunodeficiency syndrome (AIDS) surfaced and spread globally in the 1980s, continued complacency led to deterioration of the public health infrastructure supporting infectious disease surveillance and response (6). In contrast to the gains earlier in the 20th century, infectious disease mortality rates in the United States increased 4.8% annually from 36 deaths/100,000 persons in 1980 to 63 deaths/100,000 persons in 1995 (5). Even after exclusion of AIDS-related deaths, age-adjusted infectious disease mortality increased by 22% between 1980 and 1992 (7). While overall hospitalization rates in the United States declined 33% between 1980 and 1994, hospitalizations for infectious diseases declined only 12%, and the fatality rate associated with infectious disease hospitalizations doubled (8). By 1992, infectious diseases were the third leading cause of death in the United States, behind cardivascular diseases and cancer (7). In spite of overall improvements in infant mortality in Alaska during the 20th century, infectious diseases were the primary, contributing, or suspected cause of 27% of infant deaths during 1992 through 1994 (9). More than half of these deaths were associated with maternal peripartum infection.

By the early 1990s, health experts no longer believed that infectious diseases were soon to disappear. In February 1991, the Institute of Medicine convened a 19-member multidisciplinary committee to assess the status of emerging microbial threats to health. The report of the committee, published in 1992 (10), defined an emerging infectious disease as one whose incidence has increased within the past two decades or threatens to increase in the near future. The report provides an overview of the history of infectious disease emergence, identified modern demographic and environmental factors prevalent in the late 20th century that favor the emergence and spread of infectious diseases, and challenged the federal government to take action.

Preventing Emerging Infectious Diseases: A Global Strategy

The Centers for Disease Control and Prevention (CDC) responded by developing a strategy to revitalize the capacity to protect the public from emerging infectious diseases by improving four major public health activities: surveillance and response, applied research, infrastructure and training, and prevention and control (11) (Table 1). Recently, CDC updated its plan for preventing emerging infectious diseases with the publication of *Preventing Emerging Infectious Diseases: A Strategy for the 21st Century* (12) in light of new developments in infectious diseases and ongoing societal changes influencing disease emergence. To accomplish the

Table 1.

Four major areas of activity for revitalizing the public health capacity for preventing emerging infectious diseases (11,12)

Surveillance and Response

- Detect, investigate, and monitor emerging pathogens, the diseases they cause and the factors influencing their emergence, and respond to problems as they are identified.

Applied Research

- Integrate laboratory science and epidemiology to optimize health practice.

Infrastructure and Training

- Strengthen public health infrastructures to support surveillance and research and to implement prevention and control programs.

Prevention and Control

- Ensure prompt implementation of prevention strategies and enhance communication of public health information about emerging diseases.

Table 2.
Priority emerging infectious disease issues and groups of people who are at special risk (12)

Priority Emerging Infectious Disease Issues

- Antimicrobial resistance
- Foodborne and waterborne diseases
- Vectorborne and zoonotic diseases
- Diseases transmitted through blood transfusions or blood products
- Chronic diseases caused by infectious agents
- Vaccine development and use

Populations of Special Concern

- People with impaired host defenses
- Pregnant women and their newborns
- Travelers, immigrants, and refugees

goals and objectives outlined, the updated plan targets specific high-priority emerging infectious disease problems and particular groups of people of special concern (Table 2).

The updated plan emphasizes development of partnerships between health care providers, clinical laboratories, and local, state, and federal public health agencies for preventing emerging infectious diseases. Clinicians and clinical laboratory staff form the front lines in infectious disease surveillance by reporting unusual illness clusters and by providing timely information on reportable disease to local or state health departments. The clinical laboratory plays a critical role in identifying infectious agents in specimens submitted by health care providers, in assessing antimicrobial susceptibility, and in communicating these results to clinicians, infection control practitioners, and local or state health departments. State health departments collate, analyze, interpret, and disseminate these data to detect outbreaks, characterize disease transmission patterns, evaluate and implement prevention and control activities, and project future public health care needs. The state health department's laboratory conducts testing for routine surveillance, for epidemiologic studies or outbreak investigations, and for identifying rare or unusual pathogens. The updated plan proposes increasing communication between information systems by integrating surveillance systems at the CDC and by defining systems that will allow electronic data sharing between clinical laboratories, state health departments, and the CDC. The CDC provides support to state health departments and laboratories in outbreak response, reference laboratory support, and prevention guidelines. The CDC also strengthens state health departments by providing public health training for epidemiologists and laboratorians.

The CDC seeks to rebuild the public health infrastructure by providing resources to state health departments to strengthen their capacity to respond to new emerging infectious disease problems. Two such programs include the Epidemiology and Laboratory Capacity program, which provides support for core surveillance and response activities, and the Emerging Infections Program, which supports partnerships between state health departments, academic centers, and the CDC to conduct population-based surveillance and prevention research. One goal of the updated plan is to expand the Epidemiology and Laboratory Capacity program to include all state, territorial, and large local health departments (12). Additionally, the CDC supports intra- and extramural applied research, targeting the development of diagnostics, molecular tools for tracking the origin and spread of emerging pathogens, the development of new methods for assessing risk factors responsible for disease acquisition, as well as the evaluation, implementation, and long term monitoring of interventions.

Emerging Infectious Diseases in Alaska and the Arctic

Arctic populations have long endured the debilitating effects of both endemic and epidemic infectious diseases, the effects of which have impacted both social and economic development in circumpolar regions of the globe. The emergence or reemergence of infectious diseases in Alaska parallels the resurgence of infectious diseases as a threat to human health worldwide. A number of factors contribute to infectious disease emergence in Alaska and the Arctic (Table 3). The target areas outlined in Table 2 illustrate the diversity of current emerging infectious diseases issues in Alaska and all of the Arctic.

Antimicrobial resistance

In recent years, antimicrobial resistance has emerged in a number of pathogens, including *Mycobacterium tuberculosis, Streptococcus pneumoniae, Enterococcus* species, and *Staphylococcus aureus,* limiting treatment options for infections caused by these agents. In Alaska, laboratory-based surveillance first detected strains of S. *pneumoniae* with

Table 3.
Factors contributing to infectious disease emergence in Arctic communities

- Rapid population growth and crowding
- Redistribution of populations due to decreased employment opportunities in small Arctic communities resulting in urbanization of traditionally rural peoples
- Increased regional and global travel
- Mass-production and globalization of the food supply
- Changes in human behaviors such as increased substance abuse, intravenous drug use and risky sexual behavior
- Climatic fluctuations and shifts in animal insect and sea-life habitats
- Contamination of the subsistence food supply with pesticide residues with possible deleterious effects on the developing immune system
- Increased use of antimicrobial agents and pesticides, hastening the development of resistance
- Greater human contact with wilderness habitats that harbor insects and animals that may transmit unknown infectious diseases

decreased susceptibility (minimal inhibitory concentration [MIC] ≥0.1 g/mL) to penicillin and other antimicrobial drugs in the Yukon-Kuskokwim Delta region in the 1980s (13). Pneumococci with decreased susceptibility to penicillin have subsequently become widespread throughout the state. In the early 1990s, isolates with greater levels of resistance to penicillin (MIC ≥2.0 g/mL) were identified in Alaska, concurrent with increasing rates of these strains in other parts of North America (14). The emergence of drug-resistant pneumococci demonstrates that resistance is not limited to hospital-acquired bacterial infections. Drug-resistant pneumococcal infections are of particular concern in Alaska given that rates of pneumococcal meningitis and bacteremic pneumonia are up to tenfold higher for Alaska Natives than for any other population in the United States (15). A number of epidemiologic studies have shown that frequent or prolonged therapeutic or prophylactic use of antimicrobial drugs is associated with greater risk of drug-resistant pneumococcal carriage and disease (16). Studies assessing the impact of a program encouraging more judicious use of antibiotics on the prevalence of drug-resistant pneumococci in Alaska are ongoing.

Foodborne and waterborne diseases

The incidence rates of foodborne botulism and paralytic shellfish poisoning (PSP) in Alaska are among the highest reported in the world (17,18). From 1976 through 1989, 42 outbreaks of PSP accounting for 94 cases were documented in Alaska (19). The rate of foodborne botulism cases in Alaska has more than tripled from 1950 to 1997 (20). The majority of these cases have been associated with consumption of fermented foods prepared from fish or marine mammals. While improved recognition of mild cases has probably contributed to part of the observed increase in cases, modification of traditional fermented food preparation practices to incorporate modern airtight plastic or glass containers, thus creating conditions favorable for *Clostridium botulinum* spore germination and toxin production, has been proposed as contributing to the continued emergence of foodborne botulism in Alaska (21,22).

Vectorborne and zoonotic diseases

Among vectorborne and zoonotic diseases that are endemic in the United States, alveolar hydatid disease caused by *Echinococcus multilocularis* infection is the most unique to Alaska. The vast majority of alveolar hydatid disease cases in North America have occurred among residents of St. Lawrence Island and northwestern mainland Alaska (23). Untreated, mortality of alveolar hydatid disease approaches 80% (24). Foxes are the definitive hosts for *E. multilocularis* and several species of small rodents (e.g., voles) are intermediate hosts (25). Domestic dogs also may serve as definitive hosts. Infected canines excrete infectious *E. multilocularis* cysts in the stool, and infection in humans presumably occurs when these cysts are accidentally ingested. Dogs kept in close proximity to the home appear to play an important role in transmission of alveolar hydatid disease to Alaska Natives (26). Therefore, control of canine infection by regular treatment of dogs with praziquantel has been instituted in hyperendemic areas of Alaska to reduce transmission to humans (27). However, illegal exportation of infected foxes from northern

habitats to hunting enclosures in the southeastern United States threatens to spread alveolar hydatid disease outside of the Arctic (28).

Diseases transmitted through blood transfusions or blood products

In 1989, hepatitis C virus (HCV) was identified as the predominant cause of transfusion-associated non-A, non-B viral hepatitis (29,30). HCV is the most common chronic bloodborne infection, and it is estimated that 3.9 million Americans (1.8% of the population) have been infected with HCV (31). Most of these persons are chronically infected and are capable of transmitting HCV to others but may not be aware of their infection because they are not clinically ill. Therefore, the CDC has recommended HCV testing and counseling for persons at risk of infection, including all persons who received a transfusion of blood or blood products or an organ transplant before routine screening of blood donors was implemented in July 1992 (31). Improvements in donor screening throughout the United States have made the risk of acquiring HCV, as well as other known bloodborne pathogens, including human immunodeficiency virus (HIV), human T-cell lymphotrophic virus, and hepatitis B virus, extremely low (32). Injecting drug use now accounts for 60% of HCV transmission in the United States (31). A survey of injecting-drug users in Anchorage found 81% to be infected with HCV–a prevalence similar to that found in the inner city of major metropolitan areas in other parts of the United States (33). The full public health impact of transfusion-associated HCV acquired before routine screening of blood products in Alaska is poorly defined. The hidden nature of the HCV epidemic is reflected by the near doubling in number of positive HCV tests reported in Alaska, from 570 in 1997 to 1004 in 1998 (34), likely due to increased testing of persons at high risk of infection.

Chronic diseases caused by infectious agents

Several chronic diseases once attributed primarily to lifestyle or environmental factors are now known to be caused or intensified by infectious agents. Hypochromic microcytic anemia has long been found to be common among Alaska Natives despite a diet rich in bioavailable iron. In 1955, E.M. Scott and colleagues speculated that "another factor" contributed to the anemia (35). In the 1990s, it was found that fecal blood loss appeared to be a major contributing factor to iron deficiency anemia in Alaska Natives, and it was postulated that hemorrhagic gastritis, possibly caused by *Helicobacter pylori* infection may represent the bleeding source (36,37). The possible contribution of *H. pylori* infection to the higher than expected rate of gastric cancer among certain Native groups (38) requires further evaluation. Alaska Natives have high rates of chronic hepatitis B virus infection and associated hepatocellular carcinoma (38-40). Widespread use of effective hepatitis B vaccines has virtually eliminated new cases of chronic hepatitis B infection in Alaska (CDC, unpublished). In Taiwan, another area with high rates of chronic hepatitis B virus infection, universal vaccination has significantly reduced the incidence of hepatocellular carcinoma in children (41). Possible infectious agent/chronic disease associations that have been suggested in other populations have also been reported among Alaska residents, such as *Chlamydia pneumoniae* with coronary artery disease (42), human papillomavirus with cervical dysplasia (43), and Epstein-Barr virus with non-keratinizing nasopharyngeal carcinoma (44).

Vaccine use and development

Rates of *Haemophilus influenzae* type b (Hib) meningitis and bacteremia among Alaska Natives prior to routine infant immunization were the highest ever recorded (45). Routine immunization of all Alaska Native infants with a Hib conjugate vaccine began in 1991 and reduced the incidence of invasive Hib infection more than 10-fold (46; CDC, unpublished). Reemergence of invasive Hib disease after a change to a less immunogenic vaccine for routine vaccination in 1996 (47) highlights the significance of ongoing surveillance and of maintaining laboratory diagnostic capabilities for vaccine-preventable diseases, including those thought to be well-controlled. Similarly, recent school-based outbreaks of measles in Juneau and Anchorage demonstrate the importance of early recognition of epidemic vaccine-preventable diseases (48,49). Routine vaccination against hepatitis B has reduced the annual incidence of acute icteric infection from over 200/100,000 in some areas of Alaska during the early 1980s to < 1/100,000 today.

Populations of special concern

Persons immunocompromised by underlying medical conditions or immunosuppressive medications are at risk of opportunistic infection by agents that may be rare in immunocompetent populations. Through 1998, 442 Alaskans have been confirmed to have AIDS, and half of these persons have died (50). While the majority of cases have occurred

among residents of the Anchorage, Fairbanks, and Juneau metropolitan areas, cases have been diagnosed from most all areas of Alaska. Pregnant women and their newborns represent another important population vulnerable to infectious agents. Hospitalization rates for respiratory syncytial virus infection are higher for both urban and rural Alaska Native infants than for children living elsewhere in the United States (51). Each summer, more than 750,000 tourists visit Alaska. Recent outbreaks of summertime influenza A and viral gastroenteritis among tourists in Alaska and the Yukon Territory illustrate the ease with which epidemic infection can cross international borders via modern modes of transportation (52,53).

CDC's Arctic Investigations Program

In 1948, the United States Government established the Arctic Health Research Center to address public health problems in the Arctic. Over the next 50 years, this work continued under a variety of appellations and is represented today by the Arctic Investigations Program (AIP) of the CDC's National Center for Infectious Diseases. The mission of AIP is prevention and control of infectious diseases among peoples of the Arctic and Subarctic. Activities of AIP include infectious disease surveillance, descriptive and analytic epidemiologic studies, investigations of the infectious etiology of disease, development of laboratory methods, evaluation of disease prevention strategies, dissemination of public health information, logistic support of research and public health emergency response efforts by other agencies and organizations, and training in epidemiology, laboratory research, and applied public health (54). This work is carried out in collaboration with other programs within CDC and with the Alaska Native Tribal Health Consortium, native health corporations, the Indian Health Service, the Alaska Division of Public Health, foreign ministries of health, industry, and universities. AIP, with a staff of approximately 35 persons, including medical epidemiologists, nurses, laboratory researchers, biostatisticians, and support personnel, is based on the Alaska Native Health Campus in Anchorage.

With the heightened global concern of emerging and reemerging infectious disease problems, AIP, together with Health Canada, the Alaska Division of Public Health, and provincial and territorial health departments, has initiated a pilot program linking public health laboratories in Alaska, Yukon Territory, Northwest Territories, northern Quebec, Labrador, and Newfoundland to monitor invasive diseases caused by *S. pneumoniae, H. influenzae, Neisseria meningitidis,* and Group A Streptococcus. Other infectious diseases will likely be added to this system in the future.

This surveillance system allows standardization of laboratory and data collection methods, monitoring of disease rates and the emergence of antimicrobial resistance across Arctic North America, assessment of risk factors for infection, and evaluation of prevention strategies. Future collaboration with public health laboratories in other countries could complete a circumpolar network of laboratories for surveillance of new and reemerging infectious diseases in Arctic communities. In keeping with the CDC's global strategy for prevention of emerging infectious disease, the pilot program will link with other infectious disease surveillance networks to provide detection and intervention of emerging problems worldwide.

Alaska Division of Public Health

In 1945, Dr. C. Earl Albrecht became the first full-time Commissioner of the Alaska Territorial Department of Health. The first major problem facing the Department was uncontrolled tuberculosis. Dr. Albrecht became a tireless advocate for Alaska, convincing Territorial and Federal policy makers and agencies to collaborate to fight the "Scourge of Alaska." Through his efforts, surplus military buildings became sanatoria and ships became floating hospitals. During his 12-year tenure, major strides were taken towards tuberculosis control (55). Organizations such as the American Medical Association, the U.S. Public Health Service, the Bureau of Indian Affairs, and the Alaska Lung Association worked together with the Territorial Department of Health to improve case finding and ultimately provide ambulatory treatment for all Alaskans with tuberculosis. Although the names of some of these agencies have changed, many continue to work together to improve public health in Alaska.

Today, the Division of Public Health, one of seven divisions in the State of Alaska Department of Health and Social Services, continues to strive to improve the health of all Alaskans. The Division's mission is "to use the best available scientific knowledge to set public health policy and ensure provision

of services which guarantee the health of all Alaskans, so that they can live full lives with optimum well-being." The Division operates programs as diverse as epidemiology, public health nursing, emergency medical services, maternal and child health, vital statistics, laboratory services, and the medical examiner. Services provided by public health include childhood immunizations, family planning, health education, sexually transmitted diseases and HIV control, senior clinics, tuberculosis treatment, state-of-the-art laboratory testing, and epidemiology and outbreak investigations. Looking to the future, the availability of new federal funds may allow the Division to enhance surveillance for emerging and reemerging infectious diseases. Surveillance will include agents which may be used for biologic or chemical terrorist attacks.

Conclusion

The emergence and reemergence of infectious diseases during the late 20th century provide many public health lessons (56). Perhaps the most important of these lessons is the need to maintain vigilance to recognize and confront future microbial problems, including the threat of infections caused by acts of bioterrorism (57). Identification of unusual health events by astute clinicians and timely reporting to public health officials are prerequisite to investigation and control of emerging infectious diseases. In future issues of *Alaska Medicine,* the clinical, epidemiologic, and laboratory aspects of specific emerging infectious diseases of concern in the Arctic will be described in greater detail and current and future opportunities for prevention of these infections will be described. The goal of this series will be to provide timely information to clinicians and public health professionals in communities who form the front lines for identification of emerging infectious diseases and for delivery of prevention services throughout the state.

Copies of *"Preventing Emerging Infections Diseases: A Strategy for the 21st Century"* can be obtained from:

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For more information on the CDC's Arctic Investigation Program, visit the AIP website at http://www.cdc.gov/ncidod/aip/aip.htm

The Alaska Department of Health and Social Services, Section of Epidemiology website is at http://www.epi.hss.state.ak.us

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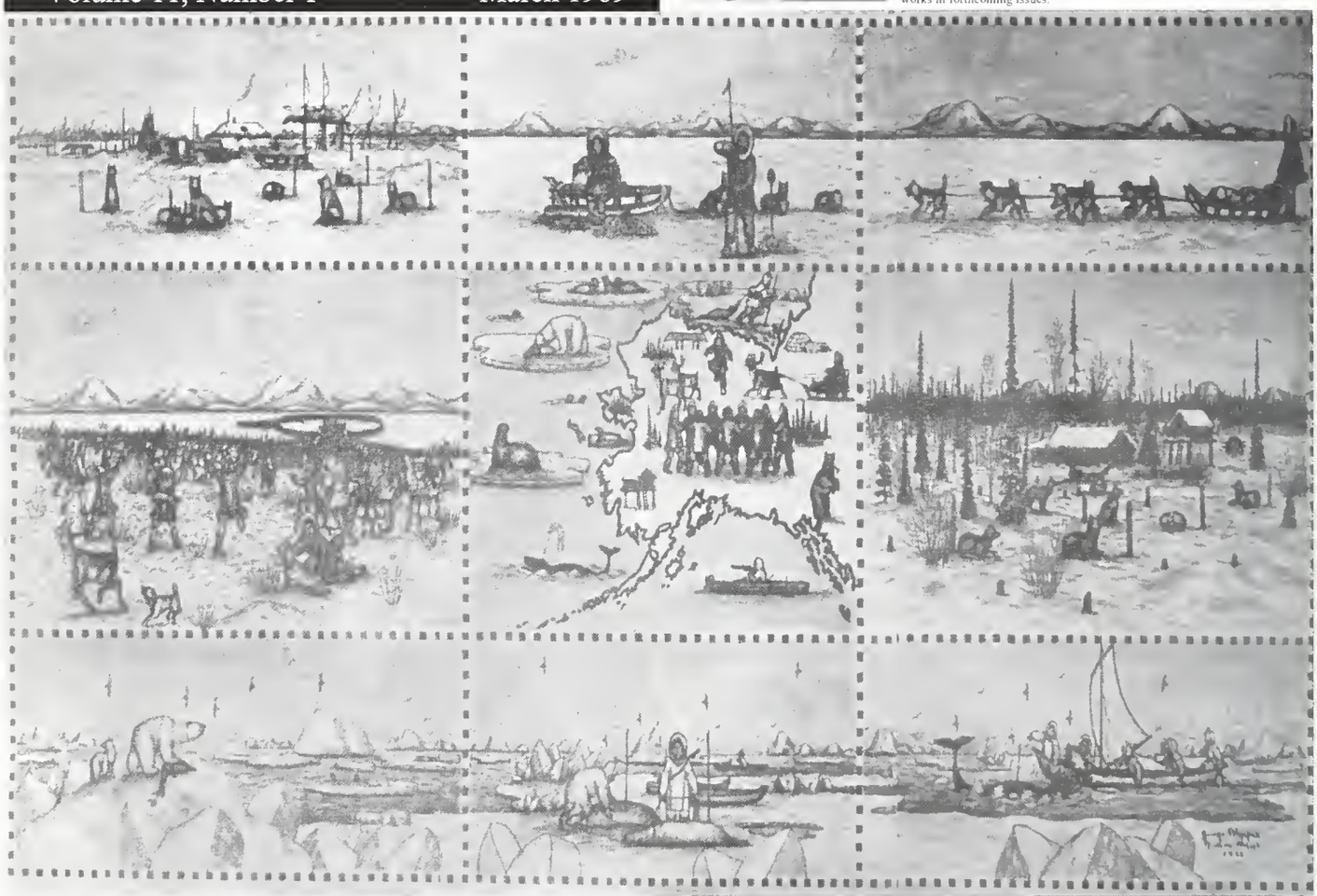
From Out of the Past — Over 30 Years Ago

Gloria K. Park, MD

George Aden Ahgupuk of Anchorage is well known for his pen and ink drawings on animal skin. Born in 1911 in Shishmaref, Alaska, Mr. Ahgupuk completed the fourth grade before joining the Eskimo men in subsistence hunting and fishing. An injury to his leg was followed by a prolonged period of hospitalization in 1934. During this time his drawings attracted much attention. Encouraged to continue his drawings, and short of paper, Mr. Ahgupuk developed his secret process for preparation of animal skins which leaves a creamy white sheet as a base for the ink drawing.

Since 1937 when his work was featured in *Time* magazine, Mr. Aghupuk has become well known. In 1948 he and his wife Kara Allockeol and their four children moved to Nome from Shishmaref, then in 1951 they came to Anchorage where he is a prominent and respected member of the art community. He presently resides at 817 W. 20th Street, Anchorage, Alaska.

Alaska Medicine is proud to have his permission to reproduce some of his works in forthcoming issues.



ALASKA Medicine

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Official Journal of the Alaska Dental Society

519 West Eighth Avenue, Anchorage, Alaska 99501

APPLICATION TO MAIL AT SECOND CLASS POSTAGE RATES IS PENDING AT ANCHORAGE, ALASKA

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APPLICATION TO MAIL AT SECOND CLASS POSTAGE RATES IS PENDING AT ANCHORAGE, ALASKA

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COBALT COMES TO ALASKA

By Shirley Cannon

Public Information Specialist
Washington/Alaska Regional Medical Program

The future for Alaskan cancer patients looks brighter this year. Thanks to dedicated people of this state who supported the Alaska Cobalt Center construction and financial drive and to the Washington/Alaska Regional Medical Program who purchased the cobalt unit.

The cobalt drive, conducted during the last 12 months, demonstrated that Alaskans have a strong concern for increased medical services in their state and that they are willing to volunteer their time, money and talents for patient care projects. It also represents a unique example of federal and private forces working together for a common cause with the full utilization of local resources.

Peter Wootton, radiation physicist, University of Washington, explains Alaska's first cobalt unit to (from left) Mary Lou Armitage, Anchorage Nurses Assn.; Elsie Blue, Alaska Hospital Assn.; Dr. George Watson, U.S.P.H.S., and Sister Agnes, Providence Hospital.

With the Anchorage medical community as the backbone of financial support, the $75,000 facility adjoining Providence Hospital in Anchorage was funded through contributions from private citizens, memorials to cancer victims, clubs, organizations and firms. Virtually every medical and paramedical group in Alaska aided in the cobalt drive and pledged continued support to the center.

The Theratron 80 cobalt unit was purchased by a $56,000 grant from the Washington/Alaska Regional Medical Program, a division of the Department of Health, Education and Welfare, which aids medical communities in increasing patient care services by fostering better utilization of manpower and resources. The local RMP, which also provides opportunities in continuing medical education established the first state-wide medical library in Alaska with the Public Health Service.

An estimated $11,000 worth of labor and building materials were donated by local trade unions and businesses. Architectural services totaling $7,500 were given free of charge and construction was done at cost.

Fund raising was done by door-to-door canvas, payroll deductions, city-wide raffle and dance, bake sales and by all other assorted projects.

Those who worked so hard to bring cobalt to Alaska were recognized at the official dedication ceremonies March 14 at Providence Hospital which featured a luncheon and public open house. Highlight of the ceremonies was presentation of a plaque in memory of Levi Browning, M.D., which was placed on the door of the cobalt center. Dr. Browning, who died of lung cancer last summer, was a former commissioner of health and welfare in Alaska and first deputy director of the Regional Medical Program in Alaska during which time he campaigned for local and federal support of cobalt for Alaska.

William Ross, M.D. who directs the national cancer control program for HEW was one of the luncheon speakers and conveyed his compliments and those from other HEW officials to the

Frank Highsmith, carpenter, was a volunteer laborer on the project.

"Hans," dachshund belonging to Ernie Matz, who supervised the construction of the cobalt center, never missed a day on the job. He also volunteered his time.

Ernie Matz, Western Construction, and James L. Sargent and Harold Johnson, local plumbers, were among local construction workers who volunteered labor for Alaska's first cobalt center.

Alaskan people for their fine achievement as an outstanding example of local initiative and leadership.

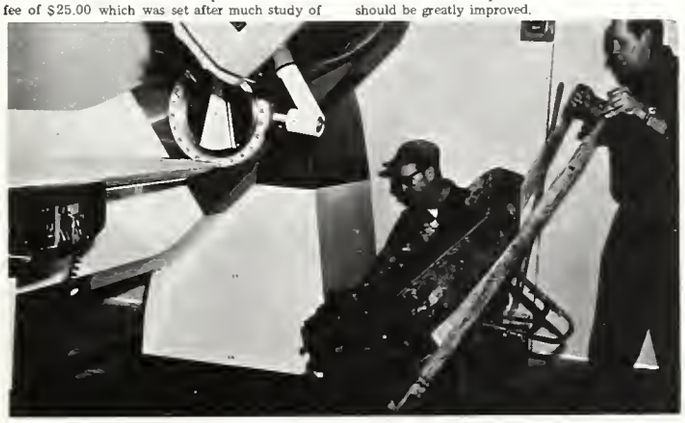
Besides representing an accomplishment for the fund-raisers, cobalt in Alaska means financial and personal benefit to cancer victims. Cancer patients will be able to remain with or near their families and jobs while receiving treatment, thus eliminating costly trips to the "outside" several times a year. Last year some 100 cancer patients had to travel to the "lower 48" for treatment according to records from the American Cancer Society, Alaska Division, and it is estimated that there were at least 200 others who sought cancer therapy "outside" on their own.

Other good news for cancer patients is that the Alaska Cobalt Center will serve all Alaskans regardless of their ability to pay. Officials at Elmendorf and Fort Richardson have asked permission from the military for their cancer patients to be treated in Alaska rather than sending them to a military facility in the "lower 48".

Since the cobalt facility is virtually paid for, the center can begin operation on a non-profit basis. Patients will not have to amortize the center as is often the case. The patient treatment fee of $25.00 which was set after much study of costs throughout the nation, will be used for operational expenses and professional fees only. Any profit generated will be used to further the state-wide cancer control program through public and professional educational programs on cancer. Extra funds may also be used to purchase new equipment, such as a cobalt source which will be needed in five years.

Alaskan physicians have known for many years that the one important modality of therapy not available in Alaska was that of high energy radiation therapy for cancer, but the need for this was even greater than anticipated. By the end of February, the first month of operation, the load was expected to be three or four patients, instead there were seven patients being treated by the cobalt center.

Besides being an important therapeutic tool, the super-voltage unit in Alaska will stimulate interest in cancer detection and therapy, and will strengthen the position to those who have been encouraging the improved data gathering and follow-up of cancer with tumor registries and associated programs. With this new and more effective cancer treatment facility, communication and patient referral within Alaska should be greatly improved.



Gene Moe, cement finisher, and Ernie Matz embed the cobalt unit in concrete, one of the final jobs in construction of the center.

Rodman Wilson, M.D.
Physician of the Year

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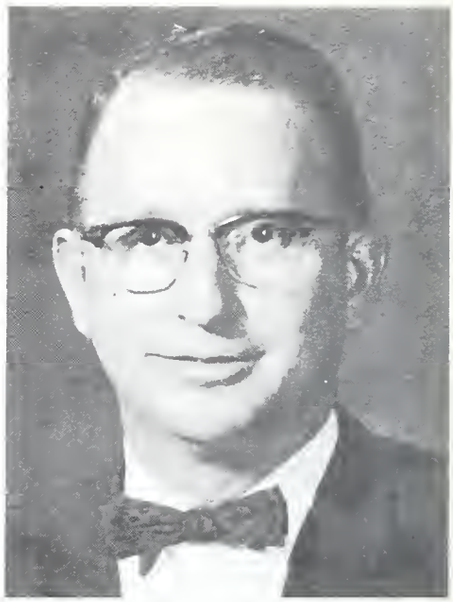

Robert Wilkins, M.D.
1969 Physician Award for Community Service

By Robert Ogden
ASMA Executive Secretary

The Twenty-Fourth Annual Convention of the Alaska State Medical Association is now history. Ninety-two physicians, sixty-three exhibitors, and seventy-two guests registered during the 4-day meeting. A number of out-of-state physicians and in-state nurses attended this year's meeting.

The Physician of the Year and the 1969 Physician Award for Community Service were the high points of the Annual Banquet. Rodman Wilson, M.D., of Anchorage was honored as the physician of the year for his work over the years in health legislation. In his presentation to Dr. Wilson, James A. Lundquist, M.D., 1968-69 A.S.M.A. President said Dr. Wilson is a "Physician's physician; one who, while guarding the integrity of the profession, seeks through legislative means to protect both his colleagues and his patients".

Robert Wilkins, M.D. of Anchorage received the 1969 Physician Award for Community Service. Over and above his busy practice, Dr. Wilkins has for years participated actively in a number of public service organizations in Anchorage, i.e. Chairman of the Health and Welfare Committee of Operation Breakthrough, a very active program of the Anchorage Chamber of Commerce; Executive Director, Anchorage Concert Association; member of the State Comprehensive Health Planning Advisory Council and State Alcoholic Advisory Council. The list goes on; it is known by those close to him that at least five nights a week are contributed to community activities.

The scientific sessions of the meeting were well attended by physicians and nurses. The program was diversified with subjects of interest to all. We were again fortunate to have very outstanding speakers.

(continued from pg 12)

From the Editor . . .

Keeping ourselves at our Professional Peak

Springtime in Alaska has brought rushing streams, warm winds, new buds, and new problems. The recent Providence Medical Center strike has demonstrated that although the Alaskan medical community is geographically far away, the Lower 48 problems have arrived at our doorstep! How we as physicians deal with this remains a challenge. At this time each independent practitioner has had to respond to the strike as our Association has prudently made no institutional decision to act as a body politic. We do need to recognize that we ourselves may confront this issue sooner than we might like to think as demonstrated by the recent New Jersey physician (private practitioners) attempt to unionize. We in the last frontier have had a proud history of independence but this tradition will be strongly challenged by the ongoing statewide business conglomeration at corporate levels and less local control of medical care options. Trying to offset these forces requires a multi-faceted approach. First and foremost is to continue providing the most efficient quality care on an individual basis thus allowing our patients no room for argument that they have a truly outstanding medical system in place. No deviation is warranted or acceptable. Second, voicing opinions using our present lobby through physician cooperatives, our state and local medical associations being the preeminent form of these.

> . . . the Lower 48 problems have arrived at our doorstep!

Strong specialty and subspecialty organizational movements would be a third mechanism of action. An excellent program would be to target the communities both here and abroad which have undergone these upheavals and the consequences. The populace Outside is now dealing with the results of these programs. Examples of decreased available technology and delays in accessibility, lack of patient/physician choice and shrinking coverage after initial grand promotional promises are active consequences.

Whether we will weather this blitz and prepare for the upcoming winter or be caught unawares is our Y2K dilemma. Let's contact our peers and associations to register our thoughts and keep abreast of the latest breaking developments. More importantly, let's keep ourselves at our professional peak.

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Volume 41, Number 3 July/August/September 1999

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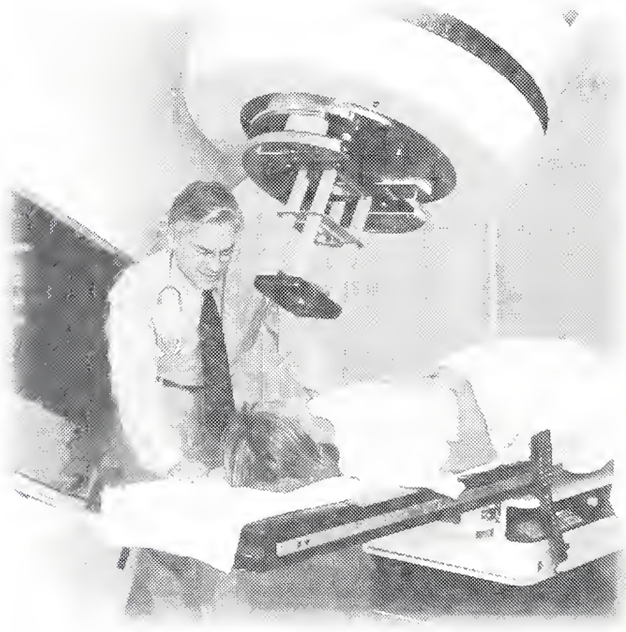

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ALASKA MEDICINE

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Volume 41 **July/August/September 1999** **Number 3**

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About the cover: Dall Ram in Denali National Park, Alaska.
Photo courtesy of Mark Newman, MD

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The Effect of Tubing Length, Gas Flow, and Number of Heaters on Maximum Gas Temperature for Aerosol Circuits Used for Cold Water Near-drowning or Hypothermia

Wayne Wallace, BA, RRT, RCP(1)

ABSTRACT

BACKGROUND: Clinicians who treat patients suffering from cold water near-drowning or hypothermia routinely warm inspire gases greater than body temperature in accordance with care guidelines promulgated by the various organizations. However, humidifiers are designed to prevent heating gases beyond 41 C (assuming the use of a standard six foot aerosol circuit) in order to meet International Standards Organization regulations (ISO). Clinicians must modify equipment in order to deliver care. There are several factors, which can effect the highest temperature that a particular circuit will achieve. Among the factors that are considered most important for maximum circuit are tubing length, gas flow, and the number of heaters (heat source). **METHODS**: The maximum temperature that a circuit could achieve was measured after varying tubing lengths (1.5 feet, 3 feet, and 6 feet), gas flow (opening or closing a venturi receiving a fixed flow rate of 10 L/min), and the size of the heat source (one or two heated humidifiers in aerosol circuit). A total of ten runs were made in each of the possible twelve combinations. **RESULTS**: Univariate statistics showed significant differences for Venturi open/close *(p=.0001)* and the number of heaters *(p=.0001)* but not the tubing length *(p=0.19)*. However, the multivariate analysis revealed significance for tubing length, number of heaters, and venturi open/closed *(p=.01)*. **CONCLUSION:** All factors (tubing length, number of heaters, and tubing length) were important determinants of maximum gas temperature. The effect of tubing length can be overwhelmed by higher gas flows.

(1) Coordinator of Clinical Studies. Barlow Respiratory Research Center, 2000 Stadium Way, Los Angeles, CA 90026-2696.

INTRODUCTION

Clinicians who treat patients suffering from cold water near-drowning or hypothermia are advised by various treatment guidelines to heat inspired gases higher than body temperature. The guidelines for cold water near-drowning issued by the state of Alaska suggest warming gases to 40.5-42.2 C as a primary rewarming technique (1); the American Heart Association recommends an inspired gas temperature of 42.0-46.0 C (2). However, the manufacturers of heated humidifiers design their equipment to meet safety guidelines promulgated by the International Organization for Standardardization (ISO). ISO standard 8185 applies to heated humidifier safety. The basic thrust of the standard is that heated humidifiers should not heat gases above 41.0 C within 50 mm of the patient outlet (3) (assuming a standard 6-foot tubing length). The current situation forces caregivers to devise methods of defeating humidifier safety systems if they desire to provide care to patients in accordance with the guidelines. Indeed, many clinicians have developed their own gerry-rigged "systems" to heat inspired gases higher than the safety systems would normally allow. Some of the more popular strategies for "beating" the humidifier are summarized below (4):

- Shortening the tubing to the least possible length practicable.
- Using tubing of the smallest possible diameter. Disabling the humidifier's safety system.
- 'Tricking' the humidifier temperature probe by placing it outside of the patient circuit.
- Adding extra humidifiers or heat sources to the patient circuit.

The purpose of this study is to look at the interaction between the number of heaters, gas flow and tubing length on maximum inspired gas temperature. As previously mentioned, clinicians have adopted many different solutions. There are numerous anecdotal accounts concerning how to warm gases greater than 41°C. Dr. Martin Nemiroff (5), a noted expert in the treatment of cold water near-drowning, actually fabricated a device using an ordinary coffee cup style heating coil and a thermos. However, there are few published reports about how to safely heat inspired gases higher than body temperature to guide the serious clinician. Which factors are most important and which factors are unnecessary?

METHODS:

Maximum gas temperatures were measured after the experimental system had been in use for at least thirty minutes. The heaters used were a Concha 1 and a Concha 2. The temperature probe was attached to the Concha 2 and connected to standard aerosol tubing of varying lengths (1.5 foot, 3 foot, or 6 foot) via a standard adapter. The alarm was taped over to permanently silence the over heat alarm. When both heaters were being tested, they were connected by 18 inches of standard aerosol tubing. In all conditions, the heater(s) were set at their maximum temperature. The gas flow was varied by either opening a standard Concha venturi to either fully closed or .60 fiO2. The same air flowmeter was used for all testing. The flowmeter was always set to 10 L/min of air and was connected to the attached venturi. Each of the twelve resulting conditions were tested ten times. The temperatures were spot-checked with standard thermometer for accuracy. The temperatures measured digitally were always within two degrees Celsius of the temperature indicated on the thermometer.

RESULTS

Univariate Analyses: The number of heaters and the Venturi status were found to be significantly associated with temperature levels (see table 1). Two heaters resulted in significantly higher temperature levels than one heater (p=0.0001) and Venturi closed produced higher temperature levels than Venturi open (p=0.0001). When analyzed without taking into account the number of heaters or Venturi status, there were no significant differences in temperature levels between varying tubing lengths (p=0.19).

Multivariate Analysis: The number of heaters, venturi status, and tubing length were each independently associated with temperature levels. Decreasing tubing lengths were associated with increasing temperature levels when the venturi was closed or there were 2 heaters (p=0.01) (see table 2).

TABLE 1.

Factor	n	Temperature °C Mean ± SD	T-test or ANOVA p-value	Analysis of Covariance* p-value
# of Heaters			0.0001	0.0001
1	60	39.7 ± 4.6		
2	60	46.3 ± 2.2		
Venturi			0.0001	0.0001
Open	60	41.2 ± 5.7		
Closed	60	44.8 ± 3.0		
Tubing Length (feet)			0.19	0.01
6	40	41.9 ± 2.7		
3	40	43.9 ± 2.4		
1.5	40	43.3 ± 7.6		

*Analysis of covariance with the other 2 factors as covariates.

DISCUSSION

The univariate analyses suggest that the most important factors were the overall gas flow through the system (venturi open or closed) and the presence of multiple heated humidifiers. There seems to be more convective heat loss associated with the higher gas flows. The univariate analysis was not significant for tubing length (p value<.19). However, there were significant differences attributable to tubing length that became apparent in the multivariate analysis. Apparently, it is possible to overwhelm the effect of tubing length with high gas flows or the lack of multiple humidifiers in the circuit.

The ramifications for clinicians attempting to rewarm patients are apparent. It is important to keep the overall flow of gas through the circuit as low as possible while still meeting the patient's inspiratory demand. This is probably better achieved using a gas blender/flowmeter combination rather than a venturi device because a gas blender would allow the clinician greater flexibility to adjust fiO2 without altering the overall flow through the circuit. Tubing lengths less than 6 foot resulted in higher overall temperatures but the effect can be easily overwhelmed by higher gas flows. Finally, the number of heaters is important to achieving higher temperatures.

It is important for caregivers that use gerry-rigged systems to exercise special precautions. The safety systems of the humidifer are being bypassed. This places the liability for patient safety rests solely upon the clinician. It is important to visually observe the patient's inspired gas temperature at all times while any such "system" is being applied on a patient. Sims et al (6) showed tracheal injuries in intubated dogs at temperatures as low 40°C. Graves and Klein (7) described "hot pot tracheitis" in a 7-year-old patient on a ventilator at only 110°F. The damaging effects of temperature on the tracheal mucosa seem to be more pronounced, according to the literature, in intubated patients. However, the clinician is cautioned not to exceed the temperature guidelines recommended by the American Heart Association or the State of Alaska. Hudson and Robinson (8) studied the difference between inspired gas and concluded that the maximum theorectical rewarming rate is 0.2° C /h, based on thermodynamic principles. Finally, Martin Nemiroff MD, a strong advocate of this rewarming strategy, does not view heating gases higher than body temperature as a primary rewarming technique, but "a stabilization technique" (9).

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(continued on pg 68)

TABLE 2.

# of Heaters	Venturi	Tube Length (feet)	Temperature °C Mean ± SD
1	Open	6	38.3 ± 1.6
		3	40.8 ± 0.6
		1.5	30.8 ± 1.0
	Closed	6	40.8 ± 0.6
		3	42.9 ± 0.6
		1.5	44.6 ± 1.0
2	Open	6	43.8 ± 0.4
		3	46.1 ± 0.6
		1.5	47.4 ± 0.5
	Closed	6	44.8 ± 0.4
		3	45.7 ± 1.7
		1.5	50.2 ± 0.4

EXPIRED GAS ANALYSIS OF FIELD SIMULATED CPR

Roy Loewenstein, BS[1]

ABSTRACT

The concentration of expired oxygen and carbon dioxide that a rescuer may give during cardiopulmonary resuscitation was originally determined without adjusting for conditions that can exist in real life. This study was devised to investigate how simulated field conditions might effect the concentrations of these gases that a rescuer would give a victim. The expired gases were measured from volunteers who performed one person cardiopulmonary resuscitation on manikins for two minutes. They then stopped the resuscitation, walked or ran 200 meters, and performed another two minutes of cardiopulmonary resuscitation while listening to loud ambulance sirens. For the thirty-eight volunteers that were tested, it was found that the percentage of carbon dioxide increased by an average of 11% and the oxygen concentration only changed by a negligible amount. This amounted to a statistically significant increase in the carbon dioxide concentration ($p<<0.01$), without a significant change in the oxygen concentration ($p>0.05$). In conclusion, exertion before performing CPR will cause an increase in the percent of CO_2 expired, while not affecting the concentration of O_2.

INTRODUCTION

There is currently a controversy over the role of mouth-to-mouth (MTM) ventilation in cardiopulmonary resuscitation (CPR) (1-6). The primary question is, which is better, chest compressions alone or with periodic ventilation? The current guidelines stipulate that, in the absence of supplemental Oxygen (O_2), CPR should be performed with regular MTM ventilations (or mouth-to-mask if it is available) (7). However, many studies have shown the majority basic life support (BLS) trained providers are hesitant or even unwilling to provide MTM because of fear of contamination (4,8,9). In addition, there is evidence that MTM ventilations during CPR is not associated with a better outcome and in some cases a worse outcome, although most of the studies were done on animals with significant differences in anatomy (10-14).

The proponents of performing only chest compressions argue that the lack of a clear benefit for MTM ventilations is due to the combined effect of altered cardiovascular parameters and the hypoxic and hypercarbic gas that is given to the victim (2). Ambient air has an O_2 concentration of 21% and carbon dioxide (CO_2) content of 0.03%. This is significantly different than the 16.4% O_2 and 4.0% CO_2 concentration that Wenzel et al measured during one person CPR (15). However, when those concentrations were measured there was no attempt to simulate the exertion and excitement that can exist in a real situation. The question then becomes, would effort and stress affect the concentrations of expired gases? In addition, a review of the current evidence of chest compressions without MTM was preformed, and recommendations were given.

MATERIALS AND METHODS

The institutional review board (IRB) at the University of Alaska, Anchorage, approved the experimental protocol of the study. Thirty-eight individuals that were certified in basic life support through the American Heart Association (AHA) volunteered and signed a consent form approved by the IRB.

Each volunteer was fitted to a mask (Survivair, Santa Ana, CA) that was attached to a breath-by-breath gas analyzer (Medical Graphic Corporation model 76004, St. Paul, MN) with a response time of 0.08 s. While they performed one-person CPR on a manikin (Laerdal Medical Corporation, Armonk, NY), their exhaled gases were measured when they stopped compressions and placed by their head by the manikin's head and exhaled. This was done for eight cycles of 15 compressions and two breaths, which lasted approximately two minutes. On one of the exhalations the percent oxygen was recorded and on the other the carbon dioxide was recorded. In contrast to the

(1) University of Washington Medical School. Study was performed at the University of Alaska, Fairbanks. Send reprints to: 4145 11th Ave NE #24, Seattle, WA 98105

previous study there was no coaching on how CPR was performed, on the assumption that the BLS providers were performing the same as they would in the field (15).

After two minutes of CPR, the mask was removed and they were instructed to go 200 meters "as fast as they would if this was a real situation;" some walked, but most jogged or ran. When they came back to the manikin, a cassette tape of ambulance sirens varying in tone was played. The volunteers put on the mask again, and did another two minutes of CPR while their exhalations were measured in the same fashion as before.

For each subject, the average values for the pre- and post-intervention was calculated and compared. The averages, the confidence intervals, and a two-tailed homoscedastic t-test were calculated for the data.

RESULTS

Thirty-eight volunteers (14 women [37%]) performed two minutes of one-person CPR before and after exerting themselves. The average age of the participants was 31 +/_9.8 (average +/-standard deviation) years old, and the average body mass index was 26 kg/m^2 +1/_4.4. Many of the volunteers were recruited from local fire departments, while others had no official health field affiliation other than possessing a BLS card. Many of the subjects possessed a subjective greater than average fitness level.

The average value for expired oxygen was 15.8 +/_0.72% before the simulation and it was 15.8 +/_ 0.66% after. The difference was found for each subject and pooled. The average of this pooled data was found to be -0.011 +/_0.70%, and the 95% confidence interval ranged from 0.21 to -0.23. When compared directly with a two-tailed homoscedatic t-test, the p-value was calculated to be 0.92. The null-hypothesis could not be disproved, and therefore the difference was not statistically significant.

For carbon dioxide, the averages for before and after were 4.11 +/_0.44% and 4.58 +/_0.51% respectively, a 11% increase. The pooled average difference was 0.46 +/_0.34%, and the p-value for the direct t-test comparison was $4.6*10^{-10}$, a highly significant difference. Figure 1 illustrates the magnitude of CO_2 concentration changes for the population.

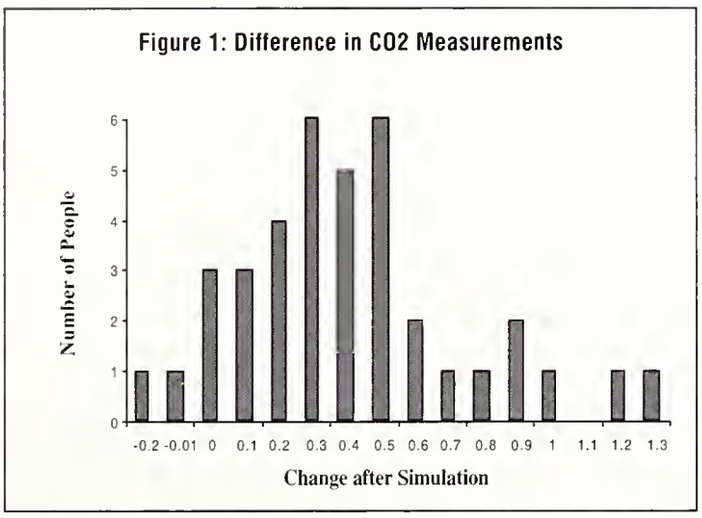
DISCUSSION

The concentration of expired CO_2 is significantly increased when simulating conditions that can exist in the field. The strength of the apparatus and experiment design was the ability to precisely measure the changes in exhaled gases. Unlike Wenzel et al the expired gases were not collected in a bag and analyzed separately, a method that would likely result in a higher accuracy of the absolute concentration determination (15). Since the data from each volunteer obtained during the simulation were compared to the baseline values for that individual, a precise measurement of the change could be obtained. While this study design emphasizes the change in concentrations instead of the absolute value, the differences in the baseline values of 15.8% O_2 and 4.11% CO_2 are quite similar to the values of 16.4% O_2 and 4.0% CO_2 that Wenzel et al found (15).

This study has tried to simulate the distance (200 meters) and the stress (the ambulance sirens) that a rescuer could face. Certainly, there are situations when the rescuer must walk five feet while others must run a mile, but these conditions have attempted to reconstruct a more "moderate" situation. A two-minute cutoff was used for measuring expired gases because a previous study determined "the initial 2 min assessment reflects the resuscitators ability to perform CPR over a longer period" (16).

The findings of this study raise several important questions. Is the the increase in CO_2 significant? Do these concentrations of expired gases affect outcome in bystander-initiated CPR? Should chest compressions alone be a recommendation of the American Heart Association? Before these and other questions can be addressed it would be useful to review current literature on the subject.

Just how good is MTM ventilation with CPR? The literature is divided on this topic. Recently there have been many studies done with animals on this topic. In swine, Berg et al could not detect a difference when CPR was applied with and without ventilatory support when measuring hemodynamics, 48-hour survival or the neurologic outcome (11). In another study, also done with swine, 7 out of 11 animals receiving positive pressure ventilation and 8 out of 11 animals without mechanical ventilatory support were successfully resuscitated (12). In dogs,



performing chest compressions alone maintains an O_2 saturation greater that 90% for more than four minutes (17). Not all animal studies have been consistent with these results. With pentobarbital-anesthetized pigs it was found that passive air movement during chest compressions was not much better than that of a blocked endotracheal tube (18). Another group also concluded that chest compressions alone were not adequate to maintain respiratory exchange after using pancuronium to paralyze pigs (19). That group was later criticized for using a drug to paralyze that "precluded spontaneous gasping," since gasping has been shown to be a significant source of ventilation in many animal trials (10,11,22-23).

Do animal trials accurately reproduce what happens in humans? Unfortunately, the majority of animals that have been used (rats, swine, and dogs) to determine the efficacy of using only chest compressions have straight airways that do not obstruct, unlike humans (5). The spontaneous gasping observed in many animal trials does not occur in humans to any significant extent, due to the pharynx becoming blocked (24,25). In one study by Safaret et al the amount of air exchange was measured during "rhythmic sternal pressure" and found that if the head was not supported, no tidal exchange occurred. Even if an endotracheal tube was inserted, the average tidal volume was found to be only 156mL (25). The difference between this value (156 mL) and the results from animal studies is probably due to the more elastic and compliant thoraces in animals (2). Due to these anatomical differences, the findings of the animal studies where spontaneous gasping play an important role in the animals' resuscitation should be interpreted with caution.

Although there has been no prospective studies looking at the effect of different O_2 and CO_2 concentrations on the efficacy of CPR in humans, there have been studies looking at the effect of expired air on paralyzed people. In several studies, which are unlikely to be repeated due to ethical constraints, volunteers and patients were paralyzed (the patients were mostly postsurgical) and the effect of ventilation with expired gases was studied. Using expired air to ventilate was associated with both adequate oxygenation and CO_2 elimination (27-29). During 30 minutes of mouth-to-mouth in one subject paralyzed with curare, tidal volumes greater than 1 L at 12 breaths/min resulted in alveolar CO_2 concentrations between 4% and 5% (lower than normal), while the O_2 saturation remained higher than 97% (24).

Is there a difference between efficacy of using expired gases in respiratory failure and in cardiovascular failure? Since there are no prospective experiments that evaluate the response of ventricular fibrillation to expired gases in humans (and for ethical reasons there never should be); indirect data must be used to arrive at a conclusion. Starting in 1983, Belgium began registering all cardiac arrest events. When the data was analyzed for the years 1983 to 1987, it was found that chest compressions with MTM resulted in a 12% long-term survival (defined as being awake 14 days after CPR), while chest compressions alone resulted in a 9% long-term survival (5). This difference was not found to be statistically significant. Later, the years from 1983 to 1989 were analyzed to see what affected long-term survival, it was found that correct CPR was associated with 16% (13-19%) long-term survival, compared to only 10% (7-14%) long-term survival when only chest compressions were used (30). It is interesting to note that if CPR was not performed there was only a 7% (6-8%) chance of long-term survival, and if only MTM was performed there was a 2% (0-9%) probability of long-term survival.

Independent of a gasping animal, does a hypoxic and hypercapnic gas adversely affect the cardiovascular system? Would it make a difference if rescuers had to exert themselves before performing CPR? In rabbits both hypoxia (18% O_2) and hypercapnia (20% CO_2) depress myocardial contractility in acute respiratory failure and may lead to cardiogenic shock. It took 10-15 minutes for this level of hypoxia to decrease isometric force by 53%, while it took only 2-3 minutes for the hypercapnic gas to depress the myocardium the same amount (31). In a cardiac papillary muscle of a cat bathed in either a 4.67% or a 9.79% CO_2 solution, it was found that the higher concentration of CO_2 depressed the contractile force, while the lower concentration enhanced it compared to control (32). This increase in the contractile force has the potential to be deleterious due to an increase in the O_2 demand of the cardiac muscle.

Before these results can be applied to humans it is important to know that hypercapnia causes greater cardiovascular depression, negative inotropy,and decreased response to catecholamines in both humans and swine than in some other species (12). There have been many studies that have looked at the effect of hypercapnia on healthy humans. Many of these studies examined the long-term effect of low levels of CO_2 (1-3%) that can be found in submarines (33). More acute exposures of CO_2 have found that breathing a 5% CO_2 concentration causes increases in the systolic BP (10-18mmHg), diastolic BP (4-10mmHg), pulse rate (8-18 beats/min), respiration rate (5-9 /min), and anxiety (34). A 6.5% CO_2 and 20% O_2 gas caused an average of a 35% increase in the mean muscle pO_2, and this was thought to be caused by an increase in the capillary blood flow, not a response to the higher arterial pO_2 from

hyperventilating (35). Another study concluded that CO_2 levels greater than 5.5% cause a decrease in the capacity for reasoning, but was probably not associated with any permanent impairment (36). Just how much information can be used from these studies on healthy subjects when discussing cardiovascular arrest is unknown. At this time, there is not enough evidence to conclude that the increased CO_2 after stress will result is a compromised outcome; more studies are needed in this area.

Perhaps more importantly then the cardiodepressive effect of the hypoxia and hypercapnia in exhaled air, is the reluctance of many individuals to perform MTM because of the exposure to body fluids (4,37). In one survey, 15% of 975 people on the University Heart Center, University of Arizona, Tucson, mailing list said that they would provide chest compressions with ventilation to strangers. 74% would perform these on relatives or friends (7). In the presence of vomitus, secretion and infection, only 13% of 70 hospital staff members would perform mouth-to-mouth; 59% would perform mouth-to-mask (6). These results of medical affiliated individuals differs from what was found when 42 lay-bystanders were interviewed about their experiences in performing CPR. Not one mentioned that they experienced hesitancy even when they encountered blood and vomit. However, the results are biased since the hesitant individuals probably did not perform CPR and as a result weren't included in the sample (38). It is interesting to note from the period of 1965 to 1998 there are a total of 15 English-language articles documenting cases of microbial pathogens being transmitted during CPR; four of these were meningococcus and three were HIV (39). The authors of that article, Mejicano and Maki, concluded that the benefits of conventional CPR "greatly outweighs" the risk of secondary infection.

In conclusion, what should the AHA Emergency Cardiovascular Care Committee recommend after they formally review the literature and publish updated guidelines in the year 2000? This author believes that there is insufficient evidence that agrees with the view that the traditional ABC's should be replaced with only chest compressions. This author also believes that there is enough evidence to corroborate the belief that chest compressions are better than nothing. The simplicity of using only chest compressions alone could lend itself to mass advertising aimed at elder individuals with cardiovascular disease and their families, a group that is significantly less likely to be familiar with CPR then the average public (40). The teaching of chest compressions for cardiac arrest in individuals who aren't familiar with CPR could become another link in the "chain of survival."

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Special Feature from the CDC . . .

The Challenge of Ongoing *Haemophilus Influenzae* Type B Carriage and Transmission in Alaska

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ABSTRACT

Cases of invasive *Haemophilus influenzae* type b disease in Alaskan children quickly dropped 10-fold after widespread vaccination with a conjugate vaccine (PRP-OMP) began in 1991. However, reemergence of invasive disease in 1996-97 soon followed a change to a combination diphtheria-tetanus toxoid-pertussis/*H. influenzae* type b vaccine which incorporates a different conjugate vaccine (HbOC). Previously unrecognized persistence of *H. influenzae* type b carriage in rural Alaska, coupled with characteristics of the immune response to HbOC, are the likely explanations for disease reemergence. The current vaccine recommendation– PRP-OMP for the first dose, followed by HbOC to complete the vaccination series – appears to protect Alaskan infants even in the face of continuing carriage and transmission. Successful control of invasive *H. influenzae* type b disease in Alaskan children will require not only appropriate immunization, but also continuing surveillance for both disease and carriage, identification of factors associated with carriage, and investigation into the feasibility of using vaccination plus antimicrobial drugs to eliminate this pathogen.

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INTRODUCTION

Before *Haemophilus influenzae* type b (Hib) vaccine became available, an average of 80-85 cases of invasive Hib disease (e.g., meningitis, bacteremia, septic arthritis) occurred each year in Alaskan children under 5 years old (1). After a universal infant immunization program against Hib using polysaccharide-protein conjugate vaccines was established in 1991, the number of Hib bacteremia and meningitis cases in children fell to an average of 3-4 each year. By the mid-1990s, it looked as though Hib disease would soon disappear in Alaska, as it did wherever widespread vaccination had been implemented (2). However, in 1996 public health officials in Alaska discovered that transmission of Hib disease was again occurring. In May of that year, four cases of invasive Hib disease were reported, and over the next 12 months a total of 10 cases occurred in Alaska Native children younger than 5 years of age.

Why did this happen?

HIB DISEASE AND HIB CARRIAGE

Hib infection can result in serious invasive disease, including meningitis, sepsis, pneumonia, arthritis, and epiglottitis. Most Hib disease occurs in infants and young children. Before vaccines became available, Hib was the most common cause of bacterial meningitis in children and the most common cause of postnatal mental retardation (3). Annual incidence of invasive disease in the US and other industrialized countries ranged from 21 to 100/100,000 for children under 5 years old (4). Children under 1 year old typically experienced the greatest rates of disease.

More commonly, Hib infection results in asymptomatic oropharyngeal carriage. Carriage of Hib can

persist for weeks to months before the infection is cleared from the oropharynx (5). In the prevaccine era, Hib carriage could be detected in 2-5% of US children under 5 years old (6). Unlike Hib disease, Hib carriage is more prevalent in older children compared to those younger than 1 year (5). Risk factors for Hib disease reflect person-to-person transmission via respiratory droplets from carriers and persons with Hib disease. These risk factors may include more siblings in the household, crowded living conditions, day care attendance, and close contact with a child with Hib disease (7-10). Disease risk within households appears to be associated with the prevalence of oropharyngeal Hib carriage among household members (11). The increased risk of invasive disease among susceptible children exposed to persons carrying Hib form the foundation of recommendations for secondary prevention using antibiotics to eradicate the organism from the oropharynx among household and daycare contacts of children with invasive disease (12).

What determines whether Hib infection leads to invasive disease? Both bacterial and host factors have been implicated. The ability of Hib to alter the sugar composition of surface lipopolysaccharides may help it breach host barriers such as the epithelium of the respiratory tract (13,14). The bacterium can also increase the amount of type b capsule produced; this may allow Hib to avoid host defenses after invasion and cause severe disease (15,16). The most important host factor for developing disease is a lack of humoral immunity to the type b capsule. Thus the greatest risk to a child occurs from the time when protection provided by transplacentally acquired maternal antibody wanes after the first few month of life until the time when natural immunity develops after exposure to other bacteria with surface antigens that are immunologically cross-reactive with Hib polysaccharide (17,18). It is this "window of opportunity" that Hib vaccines are designed to close.

THE IMPACT OF HIB VACCINES

Three Hib vaccines are licensed for infants and all contain the type b capsule polysaccharide polyribosylribitol phosphate (PRP) conjugated to a protein molecule (Table 1). Antibodies to PRP protect against disease (19), and these conjugated formulations are effective in children less than 18 months of age. Combination vaccines have also been developed for infants by adding Hib vaccine to diphtheria-tetanus toxoid-pertussis (DTP) or hepatitis B vaccines.

While completing the primary Hib vaccination series with any of the licensed vaccines provides protection, there are differences in the level of anti-PRP antibodies elicited by the conjugate vaccines following one or two doses. PRP-OMP generates a protective antibody level after the first dose, a level which is not dramatically increased by the 2nd dose. With PRP-T or HbOC, the 2nd or 3rd dose is required to achieve protection but peak antibody levels are higher than those induced by PRP-OMP (19,20). In spite of these differences in dose-response, each conjugate vaccine is protective after a full primary immunization series, and each has been used in various industrialized countries with great success (21). Early vaccination successes have lead to the goal of eliminating Hib disease among children under 5 years of age in the United States (22).

The use of Hib vaccine in the US has resulted in a 99% reduction in reported invasive Hib cases in children under 5 years of age since 1993, with 93% of 2-year-old children in 1997 having been vaccinated with three or more doses of Hib vaccine (23). Carriage surveys conducted in the US, the United Kingdom, Finland, and Iceland demonstrated the profound effect of conjugate vaccine for reducing Hib carriage (24,25), thus eliminating the Hib reservoir and providing herd immunity. Reduced carriage from vaccination has been proposed to explain decreases in invasive Hib disease exceeding the fraction of the population vaccinated, and decreases among age groups not yet vaccinated (17,26).

HIB EPIDEMIOLOGY IN ALASKA

Hib carriage and disease have been targeted by surveillance and control efforts in Alaska since the latter 1970s (Table 2). Alaska Natives have historically experienced some of the highest rates of Hib disease ever reported (28,29). The average prevaccine incidence rate for Alaska Native children under 5 years of age was 601/100,000 in 1980-82, with a peak age of onset at 6-7 months (1). This was in contrast to non-Native children of the same age in Alaska who had a rate of 128.6/100,000 and a peak incidence at age 8-9 months. Prevaccine Hib carriage rates in southwestern Alaska Native children were 5-7% (30,31).

The effect of vaccine on Hib disease has been as dramatic in Alaska as elsewhere (Figure 1). After a successful demonstration project using PRP-OMP in a combination passive-active immunization schedule in southwestern Alaskan infants (32), and demonstration of this vaccine's efficacy in American Indians in the southwestern US (33), Alaska recommended a routine primary vaccina-

Table 1. Currently licensed conjugate Hib vaccines for use in children 6 weeks of age or older.*

	Single Target Formulation		Combination Formulation		
PRP Vaccine	Protein carrier	Trade Name†	Combined with	Trade Name	Manufacturer
HbOC	Mutant diphtheria toxoid	HibTITER®	whole cell DTP	Tetramune®	Wyeth Lederle Labs
PRP-T	Tetanus toxoid	ACTHib®	- - -	- - -	Pasteur Merieux Connaught
PRP-OMP	*N. meningitidis* group B outer membrane protein	PedVaxHIB®	Hepatitis B vaccine	COMVAX®	Merck Sharpe & Dohme

*Other formulations, PRP-D (ProHIBit®), DTaP/PRP-T (TriHIBit®), PRP-T (OmniHIB®), and PRP-T/DTP (DTP/ACTHib®) are not currently licensed in the United States.
†Use of trade names is for identification purposes only and does not imply endorsement by the U.S. Public Health Service.

Table 2. Surveillance and vaccination against Hib in Alaska.

Year	Event	Reference
1977	carriage survey, southwest Alaska	30
	retrospective incidence analysis, southwest Alaska 1971-77	
1977-80	prospective surveillance, southwest Alaska	30
1980	statewide prospective surveillance program begun	1
1982-83	carriage survey, southwest Alaska	31
1984-87	vaccine trial with PRP-D	27
July 1989	passive immunization of infants in southwest Alaska with BPIG	32
Jan. 1991	statewide vaccination with PRP-OMP	32
	southwest Alaska, BPIG* at birth and PRP-OMP immunization	
May 1992	BPIG passive immunization discontinued	32
Jan. 1996	statewide vaccination with DTP/HbOC	34
May 1997	carriage survey, southwest Alaska	35
Sept. 1997	first dose PRP-OMP, HbOC for remaining doses	37
1998	carriage surveys, Anchorage and northern Alaska	AIP†

*BPIG = bacterial polysaccharide immune globulin

†CDC Arctic Investigations Program, unpublished data.

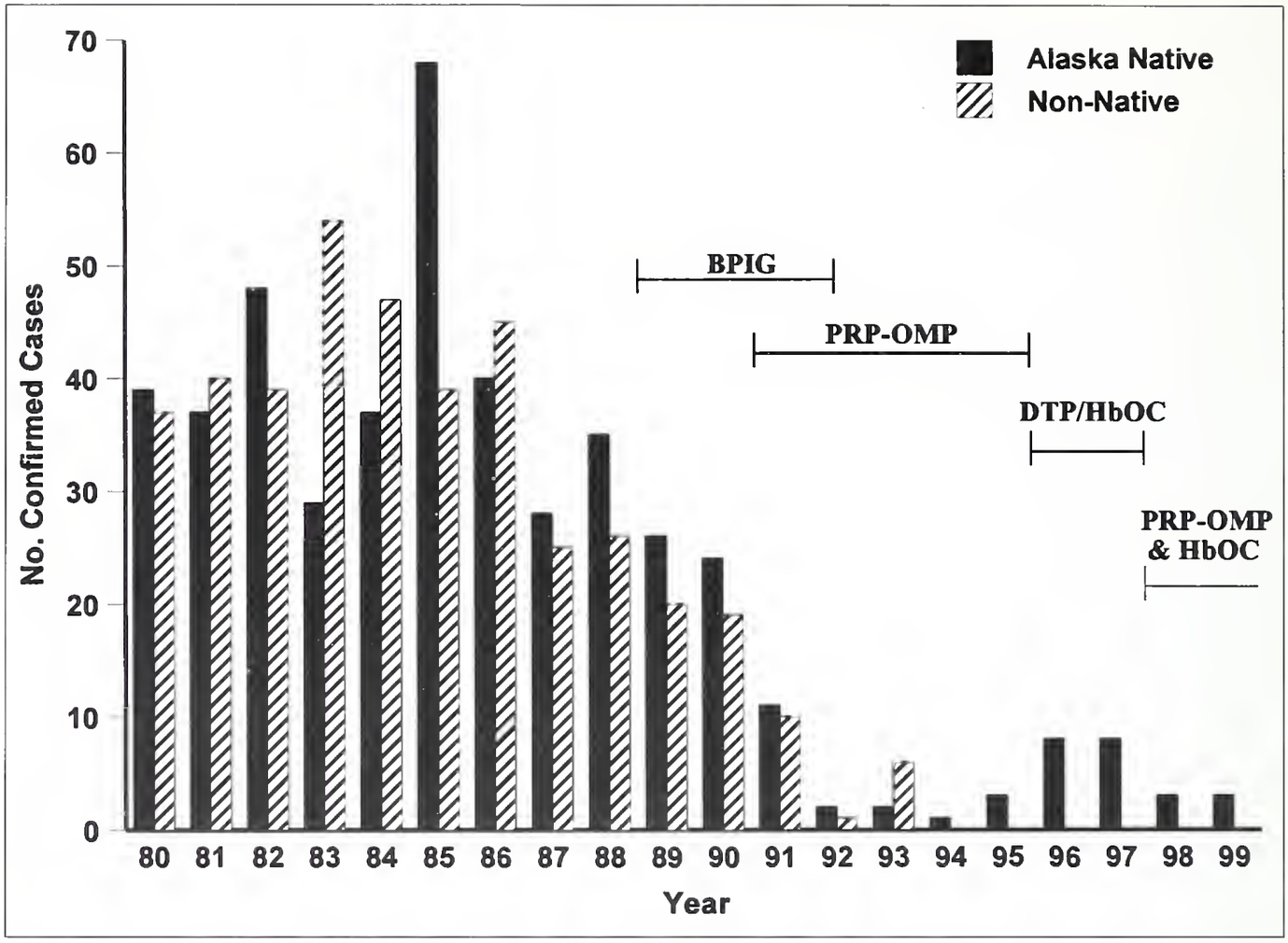

Figure 1. The annual number of confirmed cases of invasive Hib disease in Alaskan children under 5 years of age, from January 1980 to May 1999. The bracketed lines indicate the time periods for each Hib immunization schedule used in Alaska. See text and Table 2 for immunization details. Black bars, cases in Alaska Native children; hatched bars, cases in children other than Alaska Native.

tion schedule using PRP-OMP for all three doses.

WHY DID HIB REEMERGE IN ALASKA?

In January 1996 Alaska changed its vaccination policy from using PRP-OMP to using DTP/HbOC in an effort to reduce the number of injections received by children (34). Although HbOC was not expected to provide complete first-dose protection in Alaskan infants (20), low disease rates combined with vaccine effects on carriage observed in other populations indicated that transmission should be low or nonexistent in young Alaskans. However, the reemergence of Hib disease among children who had received one or two doses of DTP/HbOC was the first warning that vaccination had not reduced Hib carriage rates among Alaska Natives (35).

Oropharyngeal swabs for culture were collected from preschool children in southwestern Alaska in May 1997 (35). Carriage rates ranged from 6.1 % in 1-year-old to 14.7% in 5-year-old children, with an overall rate of 9.3%, even though 98% of the carriers were fully vaccinated. In addition, the reemergent invasive Hib isolates had the same molecular characteristics as most of the carriage isolates (36). An unrecognized and unexpected reservoir of Hib therefore remained among the Alaska Native population, allowing breakthrough cases in susceptible children. Of 16 invasive Hib cases reported during 1996 and 1997, most occurred in appropriately vaccinated children–6 were in under-immunized children (un-immunized or partially immunized children greater than 1 month overdue for a Hib vaccine dose), 6 were in children partially but age-appropriately immunized for Hib, and 4 were in children who had completed a primary vaccination series.

In response to the increase in cases and continuing Hib carriage, Alaska modified its vaccination

policy in September 1997 to ensure the earliest possible protection for infants. The current immunization schedule calls for PRP-OMP for the first dose, followed by HbOC for the remaining doses (37). This combination also stimulates higher antibody levels than other combinations tested (19). After this regimen was fully implemented, rates of disease have again fallen and the majority of cases have occurred in under-immunized children. From October 1997 through June 1999, there have been 6 cases of invasive Hib infection in children under 5 years of age, and 5 of these cases were in under-immunized children.

IMPLICATIONS FOR HIB ELIMINATION

The impact of disease prevention efforts at the regional and global levels can be categorized using the following five terms: control, elimination of disease, elimination of infection, eradication, and extinction (Table 3) (38). Although eradication of Hib appears unlikely at this time, many experts believe that elimination of Hib disease or even Hib infection are feasible goals for two reasons. First, Hib is known to infect only humans, so there are no known reservoirs for Hib in the environment. Second, Hib conjugate vaccines are highly effective in preventing disease, provide long-lasting protection, and have interrupted transmission by preventing asymptomatic carriage (39). Although elimination of Hib infection appears to have been achieved in Finland and Iceland (39), the recent resurgence of Hib among Alaska Natives suggests that Hib elimination in arctic North America may be more difficult because of continued asymptomatic carriage and transmission despite high levels of Hib vaccination. Studies are needed to identify factors associated with asymptomatic carriage of Hib in Alaska and to determine the feasibility of combining vaccination with short-course antimicrobial drug treatment for eliminating Hib from the oropharynx of asymptomatic infected persons.

THE VALUE OF CONTINUING SURVEILLANCE

Population-based surveillance for Hib disease conducted in Alaska allowed Hib reemergence in 1996 to be recognized, investigated, and controlled. Cases of invasive Hib disease are reported to the Epidemiology Section, Alaska Department of Health and Social Services. Additionally, clinical microbiology laboratories throughout the state voluntarily submit all *H. influenzae* cultures obtained from normally sterile sites to the Center for Disease Control and Prevention's Arctic Investigations

Table 3. Hierarchy of terms categorizing the impact of disease control measures (38).

Term	Definition	Example
Control	Reduction of disease incidence, prevalence, morbidity, or mortality	Hib disease in Alaska after widespread use of Hib vaccines
Elimination of disease	Reduction to zero of the incidence of a specific disease in a defined geographic area	Neonatal tetanus
Elimination of infection	Reduction to zero of the incidence of infection caused by a specific agent in a defined geographic area	Polio in the Western Hemisphere (1994)
Eradication	Permanent reduction to zero of the global incidence of infection caused by a specific agent	Smallpox (1979)
Extinction	Agent no longer exists in nature or the laboratory	None (fate of remaining two known laboratory stores of smallpox in U.S. and Russia under continued debate)

Program, where the serotype and antimicrobial susceptibility of each isolate is determined. Additional molecular and genetic studies on submitted Hib isolates are performed as needed. Periodic oropharyngeal carriage surveys will augment disease surveillance programs and will be valuable for monitoring the total Hib burden on Alaskan children and the effectiveness of any interventions undertaken to reduce this burden.

As Alaska's experience illustrates, it is especially important that surveillance continue in populations with historically high disease rates. Proper diagnosis of Hib disease by physicians is a critical component of a successful surveillance program. Diagnosis of Hib disease requires collection of clinical specimens for Gram stain and culture and use of appropriate microbiological laboratory techniques. Visualization of pleomorphic Gram negative coccobacilli in cerebrospinal fluid provides a rapid method of diagnosis. The success of vaccination has made Hib disease rare, but the ability of physicians and clinical laboratories to recognize cases of invasive Hib disease when they do occur is crucial for controlling and possibly eliminating Hib in Alaska.

THE VALUE OF PROPER IMMUNIZATION

In the vaccine era, those children at risk for Hib disease include the undervaccinated, nonvaccinated, and vaccine non-responders (23). In the lower 48 and other industrialized countries, where there is little to no Hib carriage or ongoing transmission, the various Hib vaccines and combinations can be used interchangeably in the vaccination schedule (40). In Alaska, however, the immunogenicity of the first dose must be considered because ongoing carriage presents a continuing threat of disease to underimmunized children. It is therefore critical to use PRP-OMP for the first dose, and to immunize children completely and on time.

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donation of temperature probes; and Laurie LaBree for checking the statistics and conclusions.

Products Used:
Concha 1 and Concha 2,
Hudson RCI Inc. Temecula, CA

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From Out of the Past — Over 30 Years Ago

Gloria K. Park, MD

Excerpts From *Alaska Medicine*, 1969
Muktuk Morsels

NOME

Dr. Harold Bartko has resigned from the staff of the Maynard McDougall Memorial Hospital and moved to Palmer. This again leaves Nome without a resident physician, although short-term coverage has been partially worked out.

Dr. William Carr, formerly in general practice in Valdez, has come out of retirement to practice in Nome. He is being ably assisted by Dr. Harry R. Owens who is on loan from the USPHS hospital at Kotzebue on a temporary basis. (June 1969)

Dr. William Carr has closed his general practice here and is again retired. Dr. Harry Owens who was on loan to the Maynard-McDougall Methodist Hospital from the USPHS in Kotzebue has also left the area. (Sep 1969)

Staffing problems and arrangements in this only non-government hospital in the Northern Boondocks should be of uncommon interest to the medical profession in Alaska. Despite a good (but not great) $25,000 - $30,000 salary, good and free housing, and adequate school and hospital facilities, Nome has been under-or temporarily-staffed for much of this decade.

While "private" medicine can point with pride to obvious efficiency and to individual physician responsibility to the individual patient, as well as decry along with some of the Natives, the constantly changing and not always optimal staffing of the USPHS, the fact remains that young and usually eager and well-trained physicians are regularly and reliably available to the poverty bush areas only through the USPHS.

It is evident that many physicians enter the PHS to avoid military service. Rarely do they feel their bush service time wasted, however, and a surprisingly large percentage return to the state in private practice.

A one year contract has been signed by Dr. Chung of Korea who trained in Pennsylvania and is scheduled to arrive in late December. Meanwhile, Dr. McMahon of the USPHS continues to hold the medical fort, recently supplemented by Dr. Gould of Colorado as a temporary physician volunteer.

BETHEL

Dr. Paul Eneboe of Homer, chairman of the ASMA Bush Medicine Committee, was elected (as ASMA representative) to the permanent board of directors of the Yukon-Kuskokwim Health Corporation at the organizational meeting of this O.E.O., subsidized health corporation in early August.

FAIRBANKS

Dr. William Bugh has been appointed to the State Board of Medical Examiners by Governor Miller to succeed Dr. Raymond Evans. Dr. Bugh recently had his fifth child, a boy. (March 1969)

Dr. William Bugh has closed his private office in general practice. His plans are currently indefinite. (Sep 1969)

Dr. John Noyes has a second child, first son, and has moved to Seward.

Dr. William Kinn has moved from the Fairbanks Clinic into a private office for the practice of ophthalmology.

Dr. John T. Adams of Florida has joined the Fairbanks Clinic in general practice.

Dr. Sharadkumar Dicksheet of India plans to join the Fairbanks Clinic in ophthalmology in September. Dr. Dicksheet was previously in practice in Detroit.

Dr. James Fuzzard of Florida, a board qualified radiologist has entered the private practice of radiology

at the Fairbanks Community Hospital. The hospital coronary care unit is currently enroute and will be operating shortly. Two nurses have gone to Seattle on RMP funds to get coronary care nursing instruction. The new Fairbanks Community Hospital plans are progressing but it is anticipated that it will be too small by the time the facility funded is completed, unless the USPHS will donate funds for construction of another wing on this hospital instead of building a new and less accessible hospital at Tanana. Apparently several beds in the new Fairbanks facility will be funded by the USPHS in any case but with the current oil boom funneling through Fairbanks, things can only get tighter unless more beds are funded in some way.

Dr. William Kinn has been appointed Northern ASMA Councilor by the Fairbanks Medical Society to replace Dr. William Bugh who has moved to Anchorage. Drs. Bugh and Bartko will both be replaced by new appointments to the Medical Licensing Board by Governor Miller as they are no longer in the region they were appointed from.

The new Fairbanks Community Hospital appears to be proceeding through its planning stages at a snail's pace.

GLENNALLEN

The Faith Hospital is currently undergoing expansion. A new clinic section is being added and the acute care beds are being increased from four to eight.

Dr. Chester Schneider has moved to New Jersey for a one year sabbatical from his general practice here.

KENAI PENINSULA

The Peninsula General Hospital has been taken over for completion by the Kenai Peninsula Borough which has established a hospital service district. Funds have now been allocated to proceed with modification of plans for completion of construction.

The enormous fire raging here has been on top of the news but fortunately was not a medical disaster. In fact, Dr. Elmer Gaede reported abnormally light medical demands during the blaze, apparently due to traffic restrictions and road closures. Although 80-100 miles away, Anchorage, when downwind, had very limited visibility and the choking feeling that makes our normally pure air doubly sweet. Incidentally, a good air pollution control bill (S.B.8) was passed during the last legislature (with a lobbying assist from your medical society representatives) to keep it that way.

KODIAK

Dr. Mildred McCurtry delivered a son, her first. She plans to transfer her medical office to Seldovia when a replacement is found to take over her association-type general practice here.

That great outdoor drama, "The Cry of the Wild Ram" on the life and times of Lord Baranof has completed another successful season here, with Dr. Bob Johnson prominent in the case, as usual. Dr. Johnson is also happy with his student preceptorship program and states that the new law for temporary licensure has made it much easier to get locum tenens assistance. In fact he reports many recent inquiries from willing physicians in other states.

Dr. Carl Denny, currently in the USPHS, Anchorage, plans to enter a mixed private medical practice here in January. Dr. Denny is board qualified in anesthesiology and will fulfill a great need at the new Kodiak General Hospital.

HOMER

Dr. Paul Eneboe is pleased with the way his medical student preceptorship program is working.

SEWARD

Dr. Wiley Bland of North Carolina, most recently in Anchorage with the USPHS, has opened offices in general practice here. (March 1969)

Dr. Wiley Bland is closing his office in general practice here to enter a radiology residency at Duke. Dr. Ernest Gentles is closing his general practice office here and moving to the West Coast. (June 1969)

Dr. John Noyes has moved here from Fairbanks and is opening a private office in general practice.

SOLDOTNA

Special assessment taxes are currently being paid so that work may resume on the Peninsula General Hospital. Dr. Elaine Riegel is currently doing another locum tenens here while on vacation from her pediatric residency in Iowa. The student preceptorship program here continues successful and, it is hoped, will stimulate more physicians such

as Dr. Riegel to return to medical practice in Alaska after completion of their training.

PALMER

Dr. Vincent Hume has retired from medical practice here and moved to Portland, Oregon where he plans to enter an orthopedic residency.

Dr. James Ivy is planning to open an office in general practice the first of August. Dr. Ivy served a two month locum tenens for Dr. Cunningham last summer and is currently in practice in Florida.

SITKA

Dr. Ted Phillips has announced he is leaving July 1st to accept a position in the Family Practice Department of the University of Rochester, Rochester, New York.

Dr. Dale Cloyd is leaving Petersburg to open a private office in general practice in Sitka, replacing Dr. Ted Philips.

Dr. Milo Fritz of Anchorage and Dr. David J. McIntyre of the Bellevue Eye Clinic, Bellevue, Washington, will be holding simultaneous clinics here during December.

ANCHORAGE

Dr. Robert Prouty of Cleveland, a board certified internist, has joined the Doctors Clinic. Dr. Richard Curtis has also resumed his medical practice with the Doctors Clinic.

Dr. Martin Palmer, a board qualified internist, is now in practice with the Anchorage Clinic.

Dr. Estol Belflower has closed his private office in general practice and has returned to Georgia for a residency in radiology.

Dr. Howard Romig has his 14th child, a daughter.

Dr. Edward Voke has his first son.

Dr. Grace Thompson has resigned as regional health officer in Fairbanks and has joined Dr. Royce Morgan in his general practice.

Dr. John Aase will become the Alaska coordinator of the Alaska-Washington Regional Medical Program in September. He also hopes to practice pediatrics on a part-time basis. (March 1969)

Dr. Rudy J. Leong is closing his office this summer after 11 years of general practice in Anchorage and moving to the West Coast.

Dr. James Baldauf of Pennsylvania has opened his private office for the practice of cardiology and internal medicine here. Dr. Baldauf is board certified in internal medicine and board qualified in cardiology, having just completed his training in cardiology at the University of Oregon.

Dr. William C. Compton of Cincinnati, board qualified in obstetrics and gynecology, has opened private offices here in OB-GYN. Dr. Compton recently completed his training at the University of Cincinnati.

Dr. Burl Stephens, formerly of Anchorage, has completed his medical training in Washington and is currently finishing a radiology residency at the Mayo Clinic. He plans to enter the practice of radiology in association with Dr. Bruce Wright this October.

Dr. Joseph Bloom of Boston has joined the Langdon Psychiatric Clinic. A board eligible psychiatrist, Dr. Bloom was recently stationed in Anchorage from 1966-1968 with the USPHS.

Vin Hoeman, husband of Dr. Grace Jansen, died last month in a tragic mountaineering accident in the Himalayas while attempting an ascent of Mt. Dhaulagiri previously considered impossible. Mr. Hoeman was a nationally recognized mountaineer, mountain rescue expert, and zoologist and at the time of his death was completing an exhaustive book-length study of the mountains of Alaska.

Dr. Richard Curtis has returned to general practice at the Alaska Clinic (formerly Doctors Clinic, not to be confused with The Alaskan Clinic of Fairbanks which is staffed by Drs. Storrs and Stuck).

Dr. Michael Leary Cusack of Illinois, a board eligible dermatologist has opened private offices here, doubling the skin specialist population.

Dr. Clyde F. Deal has moved his office in general surgery from the Anchorage Clinic to enter private practice at the College Medical Center.

Dr. Robert Fraser has returned to his State Tuberculosis Control position after two years in Denver. His wife Dr. Shirley Fraser plans to rejoin the Alaska Clinic in neurology, having completed her neurological studies in Denver.

Dr. John D. Gibbons of Pennsylvania has joined Dr. James Coin on the radiology staff of the Alaska Clinic. Dr. Gibbons is board certified in diagnostic radiology

Dr. Josef Kurt Mikolaschek of Colorado has joined the Alaska Clinic in general practice.

Dr. Robert E. Stelle has closed his general practice office at the Alaska Clinic.

Dr. Walter O. Tofani of New York has joined the Alaska Clinic in urology. Dr. Tofani is board eligible in urology, having graduated from the University of Zurich and completed his urology training at Long Island College Hospital in Brooklyn.

Dr. Augustin Gombart of Maryland has joined the Anchorage Clinic in general practice.

Dr. C. Jerry Little of Arkansas has joined the Alaska Clinic in general practice. Dr. Little was most recently stationed at Fort Wainwright in Fairbanks.

Dr. Rudy Leong has closed his general practice offices here. His new address is The Permanente Medical Group, 27400 Hesprian Blvd., Hayward, California 94545.

Drs. James Fraser and George Seuffert were very pleased with the student anesthesiology preceptorship program they sponsored this summer.

Dr. Joseph Wilson, USPHS Chief of Surgery, recently was awarded the USPHS Meritorious Service Medal for his contributions to the control of tuberculosis, bronchiectasis and echinococcus disease in Alaskan villages, including approximately 800 resections for tuberculosis.

JUNEAU

The Alaska Board of Medical Examiners is continuing the push for licensing law improvements, in particular the elimination of the citizenship requirement for those otherwise qualified (ECFMG), the elimination of the basic science requirement for properly qualified MDs and the speeding up of temporary permits for those qualified who wish to serve short term locum tenens tours.

Dr. Stanley Ray has his second daughter, fourth child.

Dr. Henry Akiyama organized and taught Juneau's first one month long CCU course for over 20 nurses, in cooperation with the community hospital, which now has a monitor unit installed, and the Alaska Heart Association. (March 1969)

Dr. Henry Akiyama reports that 15 of the 40 nurses who attended his weekly coronary care course from February to July have taken the final examination, with a grade average of 80. Dr. Akiyama expressed gratitude to the RMP and the Alaska Heart Association for providing course materials and audiovisual tapes. (September 1969)

PETERSBURG

Dr. Dale Cloyd of Ohio has opened a private office here in general practice. Dr. Helen Schmitt closed her temporary surgical practice here and entered medical mission work abroad.

KETCHIKAN

Dr. Arthur Wilson, Jr. has just completed a one month South Pacific medical tour. Apparently he has decided to check on the source of the flu that has decimated Ketchikan in the past winter.

Dr. James Wilson had his third daughter recently.

CORDOVA

Dr. Gayle Sacry has returned from his two month tour as a volunteer physician in Viet Nam. He reports, "My experiences in Viet Nam were very worth-while. I took care of an infectious disease ward that averaged about forty bubonic plague patients and a TB ward of 100 patients. Also I did work in the surgical department caring for casualties. I was not able to accomplish quite as much as I expected because of the slow pace at which everyone works in Viet Nam. The educational opportunity was very valuable. I certainly do not have any answers about the war, but sure know a lot more about it. I'm glad I was able to go."

Dr. Gayle Sacry reports that his student preceptee from Iowa for the past two months worked out well for both he and the student. He expects another student in a few months from the University of Colorado.

WRANGELL

Dr. David Dale has closed his general practice here and has moved Outside. Several temporary physician replacements have been arranged through RMP, but at present Wrangell needs a physician.

Letter to the Physicians. . .

Dear Physicians:

The March of Dimes and the Alaska Department of Health and Social Services are teaming up in an effort to decrease birth defects by increasing the number of women who take folic acid **before** they are pregnant.

Research indicates that a growing number of women now know that taking the B vitamin folic acid can help reduce the risk of having a baby born with birth defects of the brain and spine. However, most do not know that it must be taken before pregnancy in order to be effective. (1)

Our goal is to get more women to take the recommended daily amount of folic acid now – before they are pregnant. Achieving this goal is complicated by the fact that nearly half of all pregnancies in the U.S. are unplanned. Because of this, the recommendation is that all women of childbearing age take folic acid every day, whether or not they are actively planning a pregnancy.

Folic acid can be found in green, leafy vegetables, citrus fruits, enriched grains and cereals. Taking a multivitamin with 400 micrograms or 0.4 milligrams is a reliable way to make sure women get all the folic acid they need.

Remember that with each encounter with a woman of childbearing age as health-care providers you have the opportunity to promote preconceptional and periconceptual health. Join us in the national folic acid education campaign to prevent neural tube defects.

Dr. Peter Nakamura, Director
Division of Public Health

(1) Centers for Disease Control and Prevention MMWR Knowledge and Use of Folic Acid by Women of Childbearing Age – United States, 1995 and 1998 (April 20, 1999/48(16):325-7).

In the United States, approximately 4,000 pregnancies are affected by neural tube defects each year; 50 – 70 percent of these developmental defects could be prevented with daily intake of 400 ug of the B vitamin folic acid throughout the periconceptional period.

In 1998, the March of Dimes Birth Defects Foundation contracted with the Gallup Organization to conduct a random survey of 2,115 women aged 18-45 years. Although, more than half of the women had heard of or read about folic acid only 13 percent knew that folic acid helps prevent birth defects and mearly seven percent knew that folic acid should be taken before pregnancy. According to the survey, awareness of folic acid was lowest among women aged 18 – 24 years and women who had less than a high school education.

From the Editor . . .

Alaska Medicine Struggles

This summer has again come to the closing weeks and we have had a grand display of why we all have chosen to live in this grandest of all lands. The shortening days have us quickening our pace to get the last trips squeezed in, finish projects planned through the long winter nights, and make final Fall plans as the first snow flies.

I have had a wonderful summer and opportunities to travel our state from Prudhoe to Southeast and all the sights inbetween. We have such a treasure to preserve and protect and the resources of people and energy to continue the legacy left us by our pioneering fathers.

We in medicine are no less challenged to preserve and protect our premier medical care delivery system. Our facilities, equipment and especially expertise rival any medical center in the country. We are also breaking new ground as we continue to train our own.WWAMI continues to thrive, and our Family Practice Residency Program will graduate its first fully licensed class this academic year. We wish them all Godspeed as they head into practice in all directions.

We do have continued concerns at *Alaska Medicine* — our Editorial Board decision to decrease publication to conserve financial resources and improve article selectivity was overruled by the House of Delegates. We will continue our struggles to provide you the quality publications you have expected over the past 40+ years. We do, however, need your support to perform this task. We desperately need clinical or research articles, as well as timely surveys and case reports. We always need thoughtful and timely reviewers .

Most of all we need more articles especially from Alaskan authors. Please consider us when doing your writing and to start building a resume for our medical students and residents. Together we can continue our great tradition.

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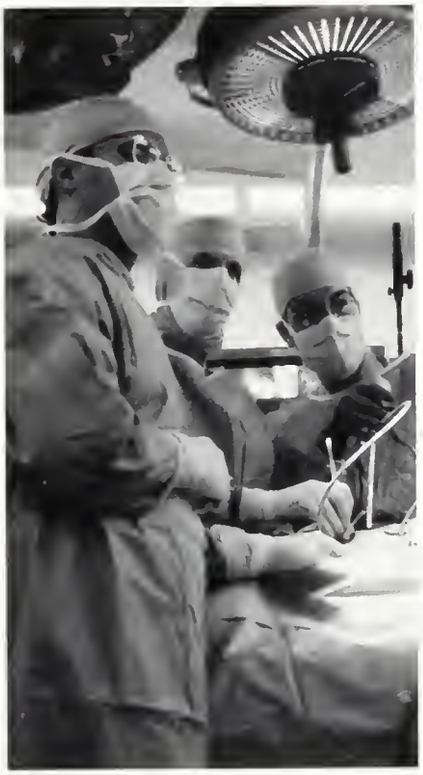

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ALASKA MEDICINE

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In this issue: **Risk Factors for Cervical Intraepithelial Neoplasm in Alaska Native Women: A Pilot Study** *by Richard MacLehose, MS, Annette Harpster, RN, Anne Lanier, MD, et al.*
Respiratory Syncytial Virus *by Thomas W. Hennessy, MD, Rosalyn J. Singleton, MD, Jay C. Butler, MD*

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ALASKA MEDICINE

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ORIGINAL ARTICLES

SPECIAL FEATURE FROM THE CDC. . .

FEATURES

About the cover: Winter Wonderland
Photo courtesy of Charles Allyson

RISK FACTORS FOR CERVICAL INTRAEPITHELIAL NEOPLASM IN ALASKA NATIVE WOMEN:

A PILOT STUDY

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ABSTRACT

Although rates for invasive cervical cancer have declined over the past twenty years among Alaska Native women, they continue to show high rates of pre-invasive cervical lesions (cervical intraepithelial neoplasia, or CIN). We investigated risk factors for CIN II/III among Alaska Native women in a pilot case-control study. Cases (n=26) included women with biopsy-proven CIN II/III, while controls (n=52) had normal cervical epithelium. The strongest risks associated with CIN II/III were HPV infection of any type (Crude Odds Ratio [OR] 8.4, 95% Confidence Interval [CI]: 2.9-29.4), HPV 16 infection (OR 40.8, 95% CI: 9.4-176.4), and a family history of cervical dysplasia (OR 3.9, 95% CI: 1.3-11.3). We also found that use of depot-medroxy progesterone acetate was associated with CIN (OR 3.0, 95% CI: 1.1-8.5). A larger investigation would be necessary to allow adequate evaluation of these, and other, risk factors for CIN among Alaska Native women.

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INTRODUCTION

Cervical cancer disproportionately affects American Indians/Alaska Natives compared to the rest of the US population. Average annual age-adjusted mortality rates for Alaska Natives/American Indians are at least double the US rate (1). Although incidence rates are available for only a small proportion of the American Indian/Alaska Native population, incidence rates are also high in areas where data are available. These geographic areas include Western Washington (2), New Mexico (3) and Alaska (4). In the Alaska Native population, invasive cervical cancer rates increased rapidly from 1969-1983 and then decreased in subsequent years. Despite this recent decrease in incidence, however, current rates still exceed the US average. Rates of pre-invasive lesions also remain elevated among Alaska Native women, as determined through examination of cytologic (Papanicolaou smear) data from clinics that serve these women (Richard Juel, MD, personal communication).

Although many risk factors for cervical cancer and cervical dysplasia have been identified in different populations (5), few studies have examined the risk factors for cervical neoplasia among Alaska Native women. A study by Davidson and colleagues, however, showed a higher prevalence of human papillomavirus (HPV) infection (21% of women, as detected by a commercial assay) among Alaska Native women than among sexually active women in the continental US (6). The data from that large study also showed that HPV infection was strongly associated with CIN, particularly types 16/18 and 31/33/35 (6). Since the time of Davidson's survey, detection methods for HPV infection have improved and now allow a more accurate assessment of HPV

detection among women with CIN, as well as among those with normal cervical cytology.

Davidson's earlier survey (6) among Alaska Native women was focused primarily on risk factors for cervical HPV infection, and was not designed to identify risks associated with abnormal cervical epithelium. To further evaluate risks associated with cervical neoplasia among Alaska Native women, we carried out a pilot case-control study of risk factors for CIN II/III among Alaska Native women attending an Indian Health Service (IHS) hospital in Anchorage, Alaska. Our pilot study was intended to demonstrate the feasibility of a larger, case-control study, and included a comprehensive examination of numerous behavioral, infectious, and dietary risks potentially associated with cervical dysplasia in this population.

METHODS

Study Subjects

Subjects were enrolled in this case-control study through their participation in the health care delivery system of the Alaska Native Health Service gynecology clinics. The clinics serve primarily Alaska Native women throughout the state of Alaska, providing routine health care needs, including Papanicolaou (Pap) smear screening tests and treatment for cervical dysplasia. This facility provides primary care for Alaska Natives who are Anchorage residents and also provides referral services for all Alaska Natives residing throughout the state.

Case women were primarily Alaska Native women (eligible for IHS benefits), aged 18-45 years, non-pregnant, with cytologic evidence of high grade cervical squamous intraepithelial lesions (or moderate/ severe dysplasia/carcinoma in situ) based on routine Pap test results. Case women were enrolled through the Colposcopy Clinic before their clinical evaluation for high grade cervical squamous intraepithelial lesions. These women were contacted upon presentation to the colposcopy clinic and invited to participate in the study as an additional part of their clinic visit. Prior to enrollment, we obtained informed consent from each subject. Subjects were asked to participate in an interview, complete a 24-hour nutrition questionnaire, provide 20 cc's of blood for serologic and vitamin assays, and undergo cervical cultures as described below. During the 14-month period of study entry, compliance with study entry among the cases was approximately 79%. Thirty-eight (38) eligible case subjects completed interviews and examinations, 10 eligible women refused.

Control women were primarily Alaska Native, aged 18-45 years, non- pregnant, with lifetime histories of all normal Pap smears. Control women were selected from the women's health clinic. Medical records, including Pap smear reports, were reviewed to document that the potential study controls had all normal Pap smears and also met the other study enrollment criteria. We selected control subjects from women who presented to the Alaska Native Medical Center Women's Health Clinic and required a pelvic examination for any reason. Compliance with study entry among control women was high: 86.4% of eligible/invited controls were enrolled. Fifty-seven (57) eligible control subjects completed interviews and examinations.

Although case women with cervical dysplasia were invited into the study based on Pap smears showing squamous intraepithelial lesions, the presence of CIN II/III on histologic examination of cervical tissue taken on the day of study entry was necessary for those subjects to be included in the analysis. Despite our focus on enrolling women with high grade dysplasia on Pap smear, 12 of the 38 (31.6%) subjects initially enrolled as cases had only atypia, nondiagnostic results, or CIN I on biopsy. We analyzed only the data from the group of cases with CIN II or III as confirmed by biopsy.

For control women who were not biopsied, we required that the Pap smear on the day of study entry be negative. Women who were selected as controls but who had atypia or dysplasia on the Pap smear on the day of study entry (n=5) were excluded from the analysis.

Interviews

A structured interview was administered that focused on risk factors suggested in previous research as relevant to development of CIN. A trained interviewer (AH) asked participants about reproductive and sexual histories, sexually transmitted diseases, hygienic practices, cervical cancer screening practices, cigarette and smokeless tobacco use, and diet. Demographic data were also collected. Dietary data were collected using a 24-hour diet recall (7). Interviews were carried out in English and lasted 30-45 minutes. The interviewer was not blinded to case or control status of the study subjects. Medical records were examined to validate responses about episodes of sexually transmitted diseases (STDs), Pap smear screening, and contraceptive use.

Pelvic Examination and Specimen Collection

Cervical specimen collection was performed during pelvic examinations for all study women.

Plastic, disposable speculums were used for the examinations. Among case women, specimen collection preceded colposcopic examination and biopsy. Specimens were collected on all women in the following order: vulvar swab for identification of HPV genome; Pap smears, fixed and air dried; endocervical swab for identification of *Chlamydia trachomatis* by polymerase chain reaction (PCR); vaginal pool swab for glass slide smear for bacterial vaginosis; vaginal pool swab for wet-mount identification of trichomonads, yeast, and clue cells under light microscopy; and cervical-vaginal lavage using 3 cc's of normal saline. Frequent glove changes were made during collection of specimens from each woman to reduce the risk of contamination of specimens. Cervical and serum specimens were immediately frozen in a -80 C freezer and sent frozen to the University of New Mexico (UNM) for laboratory analysis. Laboratory personnel were not informed as to case or control status of the subjects.

Following cervical specimen collection, case subjects underwent colposcopic examination of the cervix, which had been treated with 5% acetic acid via cotton swabs. Treatment for any abnormal conditions was provided by physicians and staff at the IHS hospital.

Identification of HPV

HPV genome was identified using a newly developed reverse blot method that employed a biotin labeled PCR product hybridized to an array of oligonucleotide probes (8). HPV genotypes 6, 11, 16, 18, 26, 31, 33, 35, 39, 40, 42, 45, 51, 52, 53, 54, 55, 56, 57, 58, 59, 66, and 68 are distinguishable using this reverse blot method. This newly developed PCR-based 'strip test' has demonstrated high sensitivity and specificity compared to more widely used consensus primer PCR techniques (8). Laboratory personnel were not informed as to the case or control status of the subjects.

Serum micronutrient assays

Blood was obtained from study subjects for analysis of red blood cell folate (9), plasma vitamin A (10), vitamin C (11), and vitamin E (10) using high pressure liquid chromatography (HPLC) techniques as previously described (10). Specimens were kept on ice before and during transport to the laboratory for processing. All sera were stored at -80 C until assays were carried out at the UNM Clinical Nutrition Laboratory.

Statistical Analysis

Data were entered into a personal computer using EpiInfo software (12). Analyses were performed using EpiInfo as well as standard packages from SAS (13). We calculated crude odds ratios as the measure of association for estimating effects of exposures and 95% confidence limits around the point estimates of effect (14). Because of the small sample size in this pilot study, we combined all patients with high grade cervical dysplasia (CIN II or III) in one case group.

RESULTS

Demographic data from the study subjects are shown in Table 1. The majority of both cases and controls reported a household income less than $20,000. The number of years of education was similar for cases and controls. The majority of case women lived in villages whereas the majority of control women lived in Anchorage ($p<.05$) (Table 1). Mean age of control women was higher than for case women ($p<.05$).

Risk factors associated with CIN are shown in Tables 2, 3 and 4. Family history of cervical dysplasia was significantly associated with CIN II/III in Alaska Native women (Crude OR 3.9; 95% CI 1.3, 11.3), while a family history of cervical cancer was not associated with case status (OR 1.1; 95% CI 0.2, 6.4). Women who had ever used foam contraception had a significantly decreased risk of CIN II/III (OR 0.3; 95% CI: 0.1, 0.9). Women who had ever used depot-medroxy progesterone acetate had an increased risk of CIN II/III (OR 3.0; 95% CI: 1.1, 8.5). The crude odds ratio associated with any HPV type (OR 8.4; 95% CI 2.9, 29.4) was statistically significant; an even higher risk was associated with HPV type 16 (OR 40.8, 95% CI 9.4, 176.4). Infection with other STDs was not associated with CIN II/III. The prevalence of HPV by type is shown in Table 5. Analysis of micronutrient levels revealed no statistically significant difference between case subjects and control subjects (Table 6).

DISCUSSION

The most important findings of this study include the strong associations between CIN II/III and cervical HPV infection, a family history of cervical dysplasia, and use of depot-medroxy progesterone acetate. Our data also showed a negative association between CIN II/III and foam contraception. We did not find significant associations with risk factors that have been identified in other studies, such as

Table 1: Demographic characteristics of the Alaska Native participants, pilot case-control study of cervical dysplasia, 1996-1997.

	Controls (n=52)	Cases (n=26)
Reason for Screening Visit		
annual exam	52 (100%)	19 (73.1%)
planned follow up	O (0%)	4 (15.4%)
suspected STD	0 (0%)	1 (3.8%)
other	0 (0%)	2 (7.7%)
Age at study entry (years)		
mean	31.3	26.8
median	33	27
Marital Status		
single	18 (34.6%)	14 (53.9%)
married/living with partner	25 (48.1%)	11 (42.3%)
divorced or separated	9 (17.3%)	1 (3.8%)
Ethnicity		
Aleut	6 (11.5%)	6 (23.1%)
Indian	21 (40.4%)	1 (3.9%)
Eskimo	22 (42.3%)	15 (57.6%)
"Lower 48 Indian*"	3 (5.8%)	4 (15.4%)
Current residence		
Anchorage	41 (78.8%)	6 (23.1%)
Areas of Alaska other than Anchorage	11 (21.2%)	20 (76.9%)
Usual residence		
Anchorage	40(76.9%)	5 (19.2%)
Areas of Alaska other than Anchorage	12 (23.1%)	21 (80.8%)
Years of education		
mean	12.9	12.0
median	12	12
range	9-18	5-15
Annual family income**		
<$10,000	12 (23.5%)	8 (30.8%)
$10,000-$19,999	12 (23.5%)	7 (26.9%)
$20,000-$29,999	10 (19.6%)	5 (19.2%)
>$30,000	17 (33.3%)	6 (23.1%)

*American Indian from a tribe in one of the contiguous 48 states.
**One subject did not report income.

cigarette smoking, sexual behavior, vaginal deliveries, or low serum micronutrients. Our inability to identify these factors as risks for CIN may relate to the small sample size of this pilot study.

Cervical HPV infection has consistently been associated with cervical neoplasia (5). Our data indicate that women with a cervical HPV were at 8.4 times the risk of cervical neoplasia as women without a cervical HPV infection. Our data also show that women with HPV type 16 were at greater than 40 times the risk of cervical dysplasia as women who are not infected with HPV type 16. Risk estimates of cervical neoplasia in women with cervical HPV infections vary substantially from study to study (5,6). Our crude estimate of the risk of HPV infection (any type) is similar to that in other studies; however, our estimate of the risk of HPV 16 infection is much larger than shown in previous reports (5,6). In a parallel case-control study of risk factors for CIN in southwestern American Indians, following a similar study protocol, we found that HPV of any type was associated with an 8-fold increase in risk for CIN II/III (Melissa Schiff, MD, personal communication). Comparable to the Alaska study, HPV 16 was associated with a 32-fold increase in risk in southwestern American Indians. Results are less consistent among studies concerning the role of other sexually transmitted diseases (STDs) and cervical neoplasia. In fact, besides the consistent HPV association, research has not demonstrated a uniform association between current infection with other STDs and cervical neoplasia (15). In our

Table 2:
Sexual and family history risk factors among Alaska Native women, pilot case-control study of cervical dysplasia, 1996-1997.

	Controls (n=52)	Cases (n=26)	Crude OR* (95% CI)**
Sexual History			
Age at first intercourse (years)			
18+	14 (26.9%)	4 (15.4%)	1
15-17	26 (50.0%)	15 (57.7%)	2.0 (0.6, 7.3)
<15	12 (23.1%)	7 (26.9%)	2.0 (0.5, 8.8)
Lifetime no. of sex partners			
0-3	9 (17.0%)	2 (7.8%)	1
4-9	20 (38.5%)	14 (53.8%)	3.2 (0.6, 16.3)
10-19	14 (26.9%)	5 (19.2%)	1.6 (0.2, 10.4)
20+	9 (17.3%)	5 (19.2%)	2.5 (0.4, 16.6)
Vaginal Deliveries			
0	20 (38.5%)	11 (42.2%)	1
1	7 (13.5%)	6 (23.1%)	1.6 (0.4, 5.9)
2	15 (28.8%)	2 (7.8%)	0.2 (0.1, 1.2)
>2	10 (19.2%)	7 (26.9%)	1.3 (0.4, 4.3)
Family History* **			
Cervical Cancer			
No	43 (91.5%)	20 (90.9%)	1
Yes	4 (8.5%)	2 (9.1%)	1.1 (0.2, 6.4)
Cervical Dysplasia			
No	31 (66.0%)	7 (33.3%)	1
Yes	16 (34.0%)	14 (66.7%)	3.9 (1.3,11.3)

* Crude Odds Ratio
** 95% Confidence Interval
*** Not all study subjects knew of family history for cervical cancer or dysplasia, hence missing values

Alaska data analysis of infection with yeast, trichomonas, clue cells, chlamydia or gonorrhea, we were unable to find any association between any of these agents and CIN. Our investigation into these factors, however, was limited by our small sample size and the lack of variation in levels of some exposures (gonorrhea, yeast). Among southwest American Indians, we have recently found that history of gonorrhea, chlamydia, or of any STD (including warts, trichomonas, bacterial vaginosis, and gonorrhea or chlamydia) was associated with a 2-fold increase in risk for CIN II/III (Melissa Schiff, personal communication).

Smoking is widely prevalent among Alaska Natives (16). A recent study, based on the Behavioral Risk Factor Survey (BRFS), found the prevalence of current smokers among Alaska Native adults to be approximately 43%, twice the state average (16). A number of studies in recent years have also implicated cigarette smoking as a risk factor for cervical neoplasia (17). Our study results, although not statistically significant, suggest that Alaska Natives who are current smokers may be at higher risk of cervical neoplasia compared with non-smokers. This observation is similar to other studies (18,19), and is consistent with promotional effects of tobacco-related components in cervical dysplasia development (17). Our companion study in the Southwest, where smoking is not common among Native peoples, did not reveal any association of cigarette use with CIN (Melissa Schiff, MD, personal communication). We found no increased risk among Alaska Natives who were former smokers or among users of smokeless tobacco.

Several investigators have reported that women with a family history of cervical cancer are at an increased risk of cervical neoplasia (20,21). While our data did not show an association with a family history of cervical cancer, we did find a significant association between a family history of cervical dysplasia and CIN among Alaska Natives. However, this information was based on reported family

Table 3: Tobacco and contraceptive use among Alaska Native women, pilot case-control study of cervical dysplasia, 1996-1997.

	Controls (n=52)	Cases (n=26)	Crude OR* (95% CI)**
History of Smoking			
Never	12 (23.1%)	4 (15.4%)	1
Past	19 (36.5%)	2 (7.7%)	0.3 (0.1, 1.9)
Current	21 (40.4%)	20 (76.9%)	2.9 (0.8, 10.2)
Smokeless Tobacco			
Never	46 (88.5%)	22 (84.7%)	1
Past	4 (7.7%)	3 (11.5%)	1.6 (0.3, 7.6)
Current	2 (3.8%)	1 (3.8%)	1.0 (0.1, 12.4)
History of OC use			
Never	8 (15.4%)	6 (23.1%)	1
Past	30 (57.7%)	15 (57.7%)	0.7 (0.2,2.3)
Current	14 (26.9%)	5 (19.2%)	0.5 (0.1, 2.1)
Foam			
Never	32 (61.5%)	22 (84.7%)	1
Past	19 (36.5%)	4 (15.3%)	0.3 (0.1, 0.9)
Current	1 (1.9%)	0	–
Ever	20 (38.5%)	4 (15.3%)	0.3 (0.1, 0.9)
depot-medroxy progesterone acetate			
Never	43 (82.7%)	16 (61.5%)	1
Past	5 (9.6%)	5 (19.2%)	2.7 (0.7, 10.3)
Current	4 (8.5%)	5 (19.2%)	3.4 (0.8, 13.5)
Ever	9 (17.3%)	10 (38.5%)	3.0 (1.1, 8.5)

* Crude Odds Ratio ** 95% Confidence Interval

Table 4: STD risk factors among Alaska Native women, pilot case-control study of cervical dysplasia, 1996-1997.

	Controls (n=52)	Cases (n=26)	Crude OR* (95% CI)**
HPV(any type)+			
negative	34 (65.4%)	5 (19.2%)	1
positive	17 (32.7%)	21 (80.8%)	8.4 (2.9, 24.4)
HPV(type 16)			
negative	34 (65.4%)	5 (19.2%)	1
positive	2 (3.8%)	12 (46.0%)	40.8 (9.4, 176.4)
Yeast wet prep			
negative	52 (100%)	26 (100%)	1
positive	0	0	–
Trichomonas wet prep			
negative	51 (98.1%)	26 (100%)	1
positive	1 (1.9%)	0	–
Clue Cells			
negative	48 (92.3%)	25 (96.2%)	1
positive	4 (7.7%)	1 (3.8%)	0.5 (0.1, 4.4)
Chlamydia			
negative	51 (98.1%)	25 (96.0%)	1
positive	0 (0%)	1 (4%)	–
Gonorrhea			
negative	51 (98.1%)	26 (100%)	1
positive	0	0	–

* Crude Odds Ratio
** 95% Confidence Interval
+ Specimen missing for one control subject

Table 5: Prevalence of HPV types by case/control status, pilot case-control study of cervical dysplasia, 1996-1997.

	Controls+ (n=51)	Cases (n=26)
PCR Assays		
Type 6	0	1 (3.8%)
Type 11	4 (7.8%)	1 (3.8%)
Type 16	2 (3.9%)	12 (46.0%)
Type 31	0	4 (15.4%)
Type 33	0	3 (11.5%)
Type 35	0	3 (11.5%)
Type 39	4 (7.8%)	2 (7.7%)
Type 40	0	1 (3.8%)
Type 42	1 (2.0%)	0
Type 45	0	2 (7.7%)
Type 51	0	1 (3.8%)
Type 52	1 (2.0%)	0
Type 53	1 (2.0%)	2 (7.7%)
Type 55	1 (2.0%)	0
Type 56	1 (2.0%)	2 (7.7%)
Type 58	4 (7.8%)	3 (11.5%)
Type 66	0	1 (3.8%)
Type 68	0	1 (3.8%)

+ Specimen missing for one control subject

Table 6: Micronutrient values among Alaska Native women, pilot case-control study of cervical dysplasia, 1996-1997.

	Controls (n=52)	Cases (n=26)	p-values
Hematocrit			
mean	38.2	39.3	p=.10
median	38.0	39.8	
range	28.5 - 44.0	31.0-44.5	
Vitamin A (mg/L)			
mean	0.40	0.42	p=.35
median	0.40	0.42	
range	0.20 - 0.66	0.24 -0.60	
Vitamin C (mg/dl)			
mean	1.18	1.10	p=.34
median	1.20	1.06	
range	0.72- 2.04	0.52 - 1.70	
Vitamin E (mg/L)			
mean	9.62	9.72	p=.87
median	9.74	8.89	
range	4.80 - 16.03	6.11 - 19.42	
RBC foliate (ng/ml)			
mean	275.9	235.4	p=.19
median	242.0	206.0	
range	78.0- 857.0	99.0 - 478.0	

history in interview, and was not documented by medical record review. In addition, reporting bias could explain this association, as case women may have been more likely than controls to ask family members about history of cervical neoplasia.

Contraceptive use has frequently been examined as a risk factor for cervical neoplasia. The most commonly reported contraceptive risk factor has been oral contraceptive (OC) use (22). Our study found no evidence in support of an association between OC use and cervical neoplasia. In the southwestern study among American Indian women, we also found no association between oral contraceptive use (ever or current use) and CIN II/III (Melissa Schiff, MD, personal communication). Another hormonal contraceptive, depot-medroxy progesterone acetate, has also received attention as a possible risk factor for cervical dysplasia (23). Our pilot study data indicate a significantly increased risk for users of depot-medroxy progesterone acetate in this population. This association may be due to actual effects of the hormones, sexual or lifestyle habits of the users, or to uncontrolled confounding. In our parallel case-control study of CIN among southwestern American Indians, we found an increased risk of (ever) use of depot-medroxy progesterone with CIN I (adjusted OR 1.8, 95% CI 1.1-2.9), but not with CIN II/III (OR 1.2, 95% CI 0.5-2.9).

We found a negative association between use of foam contraceptives and CIN. Recent studies have shown that nonoxynol-9 does not affect HPV detection (24), this result may be explained by uncontrolled confounding or other factors related to foam contraceptive use rather than to a true protective effect of foam on cervical neoplasia. Among southwestern American Indian women, no association with foam or jelly use was apparent for CIN (Melissa Schiff, MD, personal communication).

Previous studies have documented different levels of serum micronutrients among women with and without cervical neoplasia (25,26). In particular, low red blood cell (RBC) folate levels have been shown to be a moderate risk factor for dysplasia (27,28). Low levels of serum vitamin E and vitamin C have also been negatively associated with cervical dysplasia (25,26). Numerous studies have also documented an association between low vitamin A intake and certain epithelial cancers, including cancer of the cervix (29,30,25). The data from this study, however, do not show any significant differences between mean micronutrient levels in case and control subjects. However, our ability to detect differences in micronutrient levels was hindered by small sample size and subsequent lack of power. Therefore, although our data do not show any significant differences in micronutrient levels between case and control subjects, further studies including more participants may be able to detect true differences, if any exist. Our dietary data collected for this study have not yet been analyzed, and should provide additional information related to the possible role of diet and dietary micronutrients in CIN in this population.

We expected to see a large proportion of both case and control subjects who had laboratory evidence of anemia. However, the mean hematocrits of study subjects was relatively high (38.2 for controls, 39.3 for case subjects). A high prevalence of chronic anemia has been long recognized among Alaska Natives, particularly iron deficiency anemia (31-33). In a 1988-89 survey of 19 Alaska Native villages, the prevalence of anemia in all age and sex groups was nearly twice that of the US population, based on NHANES II data (32). Approximately 18% of women aged 18-44 years showed evidence of anemia in that survey. Our data may provide some evidence that the population-based prevalence of anemia in young women may have decreased in the past ten years (particularly the data from case women, who were more likely than controls to come from rural communities). This observation may warrant further evaluation through a broader, population-based perspective.

Our study has many limitations that must be recognized. A potential limitation of this study is its clinic-based scope. Control subjects were mainly from the Anchorage population, while patients with CIN were from Anchorage and other parts of the state. Expenses of travel and distance made it impossible to include controls from throughout the state. Therefore, a higher percentage of control subjects lived in the city of Anchorage and were Indian. The different demographic, ethnic and age distributions between the cases and controls suggest a potential sampling bias. Future studies with additional resources will be able to match controls to cases by community of origin.

Another limitation is the small sample size of this pilot study and the subsequent lack of adequate power for detecting associations. Recall bias is always a potential limitation in any case control study; however, we minimized the amount of recall bias by performing chart reviews to verify the answers of the participants. Subjects were also frequently reminded by the interviewer that their answers were confidential to reduce information bias regarding sexual histories. The interviewer was not blinded to case status of the subjects; however, interviewer bias was minimized by using structured interviews with detailed question-by-question instructions.

Measurements of HPV at a single time point, as was done in this study, may not reflect the true infection status of the subjects. Repeat testing of subjects for HPV has been shown to increase measures of prevalence of infection among control subjects, even in the absence of new sexual partners (34). A final limitation of this study was a lack of information on the sexual history of the subjects' partners. A partner's sexual history has been shown to be associated with cervical neoplasia (35,36).

Despite these potential limitations, our data suggest CIN II/III among Alaska Native women may be associated with HPV infection, and particularly HPV type 16 infection. Use of depot-medroxy progesterone acetate, and a family history of cervical dysplasia also appear to increase risk of CIN II/III. Our data also suggest that CIN II/III may be negatively associated with use of foam contraception. Our study was too small to clearly show if there was an association with cigarette use, although the (non-significant) association suggests a moderate risk (odds ratio 2.9) associated with cigarette use. In the future, studies with larger sample sizes and inclusion of partner sexual history would allow us to better estimate risk factors for CIN in this population.

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Special Feature from the CDC . . .

Respiratory Syncytial Virus: Current status and hope for the future

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INTRODUCTION

Respiratory syncytial virus (RSV) is the single most important respiratory pathogen in infancy and early childhood. Nearly all children will be infected by 2 years of age (1), but RSV can cause infections throughout life, particularly among the elderly or those with compromised immune systems. Approximately 40% of infected infants and young children will develop a lower respiratory infection (LRI) (2) and about 1% of these will require hospitalizations (3). In the United States there are an estimated 91,000 hospitalizations and 4,500 deaths due to RSV annually (4). The annual medical costs due to RSV hospitalizations in children is estimated to be $300 million (5), and from $150 - 680 million per year for adults hospitalized with RSV pneumonias (6).

Although RSV infections are common throughout the U. S., residents of Alaska have a high burden of RSV disease compared to other populations. Over 30 years ago, Brody reported that 35% of Alaskan Eskimo children surveyed had at least one episode of pneumonia or bronchiolitis in the first year of life (7), and Maynard, et al demonstrated a high prevalence of RSV antibodies (89%) among children in Bethel during the acute phase of a respiratory illness (8). Today, RSV is still the major respiratory pathogen among children in Alaska (9,10). In this article we will discuss the epidemiologic features of RSV infections with emphasis on RSV in Alaska and highlight new developments in RSV prevention and control.

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RSV INFECTIONS

First isolated from chimpanzees in 1956, RSV is an enveloped, single-stranded RNA virus of the family *Paramyxoviridae*. The virus infects respiratory epithelium and derives its name from the ability to induce syncytia, or epithelial cell clumps, *in vitro*. The RSV genome codes for three surface proteins, including glycoproteins mediating viral attachment (G) and fusion (F). These are the only viral components identified which induce neutralizing antibody (11).

RSV spreads easily from person-to-person through respiratory secretions. The two primary methods of transmission include direct mucous membrane contact with large droplets of secretions, such as from a cough or sneeze, and self-inoculation via hands made infectious by touching contaminated objects. The virus survives on environmental surfaces for several hours but is inactivated by soap and disinfectants. Rhinorrhea is the primary symptom of early infection in infants and develops after an incubation period of about 5 days (range from 2 - 8 days). Signs of LRI such as tachypnea, rates or wheezing can develop 2-5 days later. Severe RSV bronchiolitis is characterized by the necrosis of ciliated epithelial cells, peribronchiolar mononuclear infiltrates, submuscosal edema and bronchorrhea. this results in bronchiole obstruction, patchy atelecatasis and pneumonia. RSV is responsible for 40 - 50% of hospitalizations for bronchiolitis and 25 - 37% of pneumonia admissions (12). In a study of patients hospitalized with RSV infection, 37% of chest x-rays showed infiltrates, 18% showed hyperaeration, and 15% showed both (12). Sevcre complications of RSV infections include apnea, especially among infants younger than 6 weeks of age, and respiratory failure requiring mechanical ventilation in up to 8% of hospitalized children.

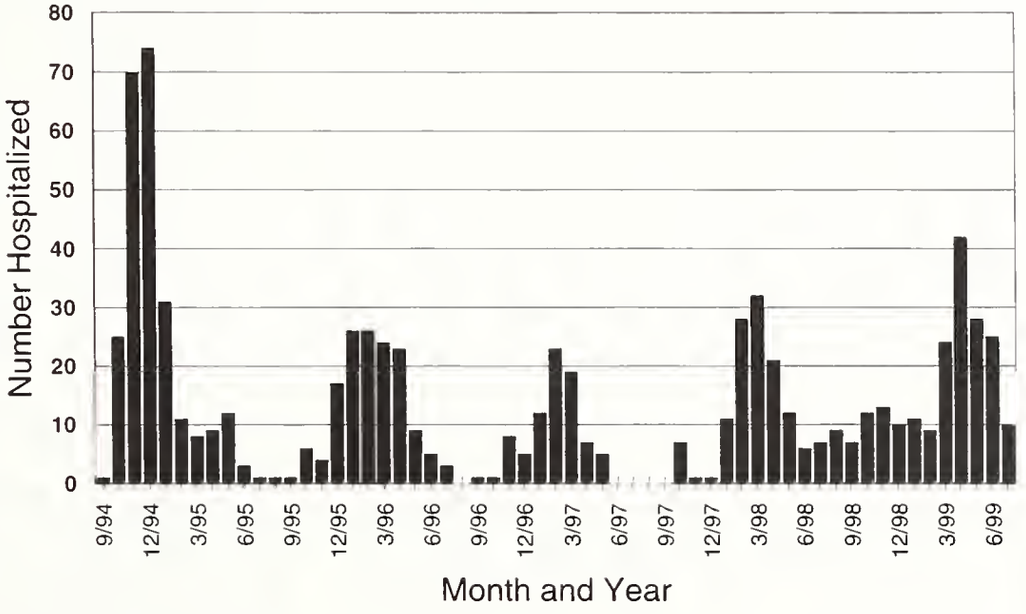
Immunity to RSV infections is a function of both humoral and cellular responses (13). Infants receive maternal RSV antibodies transplacentally and through breast milk. Antibodies to surface glycoproteins correlate with resistance to infection but such immunity is incomplete and of short duration. A study of adults with previous RSV infection showed that reinfection with the same strain could be experimentally induced in one-half of the volunteers 2 months after natural infection, and among two-thirds by 8 months (14). Multiple episodes of reinfection were common in the 26 month study, despite measurable antibody. Once infection is established, cell-mediated immunity is important in clearing RSV infection (13). Children with deficient cellular immunity may shed virus for several months after infection, compared to 7 to 21 days for immunocompetent children (13).

EPIDEMIOLOGY OF RSV INFECTIONS

In the U.S. surveillance for RSV infections is conducted through a voluntary, laboratory-based system, the National Respiratory and EntericVirus Surveillance System (NREVSS), involving 100 clinical and public health laboratories which submit specimens for antigen-detection and virus isolation to the Centers for Disease Control and Prevention (CDC) laboratories in Atlanta. In Alaska, RSV infections and bronchiolitis are not a notifiable conditions, but RSV hospitalizations among children residing in the Yukon Kuskokwim have been tracked by the CDC Arctic Investigations Program since 1991. Data from these systems indicate that the annual RSV 'season' generally runs from November through mid-May, with peak activity in January or February. However, the peak and length of RSV activity does not occur predictably within this time frame. In the YK Delta, the typical region-wide annual epidemic lasts from 5-6 months; however, sporadic cases have been reported in every month of the year, and during the 1998-99 season RSV activity did not peak until April with a continued high rate of hospitalizations through June. (Figure)

Severe RSV infections in the U. S. are most commonly seen in infants aged 1 to 6 months. Risk factors for severe RSV disease in children include prematurity, underlying medical conditions (bronchopulmonary dysplasia (BPD), congenital heart disease or immunodeficiency), age < 3 months, low RSV-antibody titers, and group A strain of virus (15). Among infants of the YK Delta who are hospitalized with RSV infection, these same risk factors are associated with severe disease (9). In addition, a case-control study among these children showed that breast feeding was associated with lower risk of RSV hospitalization, while household crowding (4 or more children in a household) was associated with a higher risk of RSV hospitalization (CDC, unpublished data).

Common sequelae of RSV infections include otitis media and subsequent wheezing. In a prospective trial of over 450 children with acute otitis media (AOM), RSV infection accounted for 39% of the viral AOM, and 74% of children with RSV upper respiratory infections had RSV detected in the middle-ear fluid (16). Several studies have documented that following RSV bronchiolitis children often develop wheezing or asthma, but have left unanswered the question of whether viral-induced wheezing and allergic asthma are causally linked (17-20). In a prospective cohort study of Swedish infants with RSV bronchiolitis and matched controls who were followed to age three, RSV infection in the first year of life was found to be an independent risk factor for asthma, especially among



Hospitalizations for RSV infections among children < 3 years old from the Yukon-Kuskokwim Delta, Alaska, August 1994 - August 1999.

children with a family history of asthma or atopy (21). Among children in Tucson, Arizona who were followed from birth to age 13 years, RSV infection was associated with a increased risk of wheezing by age 6 years; however, the risk decreased markedly with age, and the association with wheezing was not statistically significant by age 13 (22). Other factors which appear to increase the risk of asthma after RSV or other lower respiratory infections among infants include exposure to tobacco smoke (23,24) and exposure to smoke from wood-burning stoves (25).

Chronic respiratory disease, including asthma, is common among Alaska Native children. In spite of improved living conditions and improved availability of medical care, asthma is one of the few medical conditions that has not improved for Alaska Natives. In a 1997 survey of 465 Alaska Native children in grades 6-9 in the YK Delta, 24% had asthma or asthma symptoms, another 37% had chronic cough with sputum production, and only 39% were without symptoms of pulmonary disease. (Gregory Redding, MD, personal communication) Bronchiectasis is rare in other U.S. populations, but is relatively common among Alaska Natives, especially in the YK Delta. The high prevalence of bronchiectasis has continued despite control of tuberculosis, pertussis, and measles, the principal infectious diseases associated with bronchiectasis. In a recent review of 46 cases of bronchiectasis we found that the most common predisposing factor was early and recurrent pneumonias. (Singleton, unpublished data) The reasons for the high rates of these chronic respiratory diseases in the Alaska Native population are incompletely understood. CDC's Arctic Investigations Program along with the Yukon Kuskokwim Health Corporation has begun an investigation to explore the hypothesis that respiratory infection such as RSV pneumonia and bronchiolitis in infants initiate processes which result in asthma and bronchiectasis. We are evaluating children identified during the 1993-94 RSV season who were hospitalized with RSV disease and a matched group of controls who were not hospitalized to determine if differences exist in symptoms of chronic respiratory disease, pulmonary function, or intercurrent illnesses. This investigation will allow us to evaluate current infectious risk factors for chronic respiratory disease in children and assess the burden of chronic respiratory disease attributable to RSV.

Although most adult infections consist primarily of upper respiratory symptoms, RSV is an important and under-recognized cause of lower respiratory disease, especially among the elderly. In a study of community-acquired pneumonia among adults in Ohio, 4.4% of those hospitalized during mid-December through May had serologic evidence of RSV infection, making it the fourth most common pathogen identified during the winter season, behind *Streptococcus pneumoniae* and influenza virus infections. RSV-infected patients could be distinguished from those with bacterial pneumonias by their more frequent wheezing and rhonchi and by normal white blood counts (26). Nosocomial outbreaks of RSV infections among adult and pediatric bone marrow recipients have occurred during the RSV season and are associated with a high rate of mortality due to secondary pneumonias (27,28).

RSV HOSPITALIZATIONS IN RURAL ALASKA

Between 1993 and 1996 the CDC Arctic Investigations Program, Yukon Kuskokwim (YK) Health Corporation, and Johns Hopkins University collaborated to conduct active laboratory surveillance to determine RSV hospitalization rates and risk factors in YK Delta children less than 3 years of age (9). During the three study years, 68% of hospitalizations in YK Delta children < 3 years of age were for respiratory infections, and 45% of children hospitalized with respiratory infections were RSV-positive. The annual RSV hospitalization rates for infants < 1 year of age ranged from 53-262 per 1,000 infants which is 4 to 18 times higher than the general U.S. population (2-14 per 1,000), and is the highest ever reported. During the peak year (1994) one-fourth of all children in the YK Delta were hospitalized with an RSV infection. One-third of children hospitalized with RSV required transport from the YK Delta Regional Hospital to an Anchorage hospital because of the severity of illness or lack of bedspace in Bethel. Fourteen (3%) children hospitalized with RSV required mechanical ventilation, and 1 died. Of note, the peak age of hospitalization (0-2 months of age) was younger than the general U. S. populations (peak 1-5 months of age). A high proportion of children (34%) were readmitted for another acute respiratory illness during the year after the initial RSV hospitalization, and 19% of all children admitted with RSV were readmitted with at least one additional episode of RSV infection.

RSV Diagnosis and Clinical Care

Diagnosis of RSV infection can be by virus isolation, demonstration of viral antigens, detection of viral RNA, or by a demonstrable rise in serum antibodies. RSV cultures are performed only in

specialized laboratories and results usually are not available during the hospitalization. Rapid detection of RSV antigen from nasopharyngeal secretions using fluorescent antibody (FA) or enzyme-linked immunoassays (EIA) are the most common techniques used for diagnosis of RSV infection in hospitalized infants. The sensitivity of these assays range from 70% to over 90% depending on the quality of the specimen and adherence to the protocol designed for each assay. Testing of specimens obtained by nasopharyngeal wash (suctioning the nasopharynx after instilling 1-3 cc of normal saline) is more sensitive than those obtained by nasal swab (29). Reverse transcriptase polymerase chain reaction (RT-PCR) technology appears to be a promising tool for rapid and specific diagnosis of RSV infections in the future (30). Mulitplex RT-PCR may provide a tool to simultaneously test for several respiratory pathogens (31). Specific RSV diagnosis is important in hospitalized children for the purpose of cohorting patients and instituting infection control measures to reduce nosocomial RSV infections. Moreover, rapid confirmation of RSV infection may reduce empiric use of antibiotics, thus lessening the selective pressure for drug-resistant strains of bacteria (32).

Clinicians are often faced with the difficult task of deciding which children with clinical evidence of RSV illness require hospitalization. A prospective evaluation of 213 infants less than 13 months of age who had bronchiolitis demonstrated that the following six features of the initial presentation were associated with more severe illness: "toxic" appearance, oxygen saturation $< 95\%$, gestational age < 34 weeks, respiratory rate ≥ 70 breaths per minute, atelectasis on chest xray, and age younger than 3 months (33).

At this time, supportive care in the form of supplemental oxygen and maintaining adequate hydration along with cardiorespiratory monitoring are the most important aspects of the inpatient management of RSV lower respiratory infections. Bronchodilators are often used to treat RSV infection, although the data on efficacy are conflicting. A meta-analysis of fifteen randomized, placebo-controlled trials of bronchodilator treatment of bronchiolitis suggested that these agents produce only modest short-term improvements in the clinical features of mild to moderately severe illness (34). Several randomized studies have demonstrated improvement in clinical score, respiratory rate, pulmonary mechanics, oxygen saturation, and length of hospitalization when nebulized epinephrine (available as racemic epinephrine) was used as a bronchodilator rather than albuterol (35-38). Steroids, antihistamines, and theophylline have not been shown to have efficacy in the treatment of RSV bronchiolitis. The only specific drug for treatment of RSV infection, ribavirin, is not widely used today for routine treatment of bronchiolitis because of conflicting evidence for efficacy, high cost, requirement for continuous aerosalization, and concerns about possible teratogenicity for pregnant health care providers. However, it may have a role in treatment children with severe disease and those with certain conditions associated with severe disease, such as congenital heart disease, chronic lung disease, prematurity, and immunosuppression (39). To date, clinical benefit from immunotherapy for RSV infection has not been documented (40,41).

RSV is a major nosocomial threat on pediatric wards. Contact isolation precautions can prevent nosocomial transmission from persons hospitalized with RSV infection (42). Wearing gowns and gloves along with good compliance with handwashing after patient contact is recommended to decrease the incidence of nosocomial RSV cases (43). Other measures to prevent nosocomial transmission include using private rooms or cohorting patients with confirmed RSV infections, and excluding health care workers who have respiratory infections from caring for uninfected persons.

PASSIVE IMMUNIZATION

In 1997, an RSV immune globulin for intravenous administration (RSV-IVIG, RespiGAM™*) was licensed for prevention of RSV in premature infants and patients with BPD. Monthly intravenous administration during the RSV season resulted in a 41% reduction in RSV hospitalizations in infants with bronchopulmonary dysplasia or premature birth (44). In 1998, palivizumab (Synagis™*) containing a monoclonal antibody to the F glycoprotein was licensed. Palivizumab provides a number of advantages over RSV-IVIG: palivizumab is administered by intramuscular (IM) injection, measles and varicella vaccines can be administered to children receiving palivizumab (these vaccine should be delayed in children receiving RSV-IVIG because of neutralizing antibodies to these viruses in the immune globulin preparation), and because palivizumab is not derived from human immune globulin, it can be readily produced and should be free of contamination by bloodborne pathogens. In

*Use of trade names is for identification only and does not imply endorsement by the U.S. Department of Health and Human Services

a large randomized study conducted at 139 centers in the U.S., Canada, and the United Kingdom, 4.8% of infants with prematurity (birth at ≤35 weeks gestation) or bronchopulmonary dysplasia who were given monthly IM injections of palivizumab were hospitalized with RSV during follow-up compared to 10.6% of controls receiving placebo–a 55% reduction in RSV hospitalizations (45). The benefits of palivizumab are restricted to reduction in RSV-related hospitalizations as compared with RSV-IVIG, which reduced hospitalization for respiratory illness of any cause. However, palivizumab is the preferred method of passive immunoprophylaxis for most high-risk children because of its ease of administration, safety, and effectiveness (46). The American Academy of Pediatrics recommends considering monthly palivizumab prophylaxis during the RSV season for infants and children younger than 2 years of age with chronic lung disease who have required daily medical therapy within 6 months, infants born ≤28 weeks gestation up to 12 months of age, infants 29-32 weeks gestation up to 6 months of age, and immunocompromised children (46). Given the large number of infants born at 32-35 weeks gestation, palivizumab is only recommended for children in this age group who have additional risk factors. In a trial among children with cyanotic congenital heart disease, RSV-IVIG was associated with an unexpected increase in surgically related adverse events, possibly because high-dose intravenous immune globulin increased blood viscosity in these children who already had increased blood viscosity because of elevated hematocrits (47). Although palivizumab should not influence blood viscosity, its use is not recommended for children with cyanotic congenital heart disease until additional data are available from an ongoing trial among these children (46,48).

RSV VACCINES

There is no RSV vaccine available at this time although several are under development. The first RSV vaccine was developed and tested in the 1960s with discouraging results. This formalin-inactivated vaccine was found to induce only low levels of antibody and rates of severe RSV infection in infants were higher in vacinees than non-vaccines (49-51). However, a new generation of RSV vaccines are under evaluation, including live, attenuated RSV vaccines, vectored vaccines (e.g., recombinant vaccinia viruses expressing RSV proteins), and RSV subunit vaccines (52,53). Live, attenuated RSV vaccines have been shown to be immunogenic and appear to be safe in chimpanzees, human infants, children, and adults (54,55). Two vaccines directed towards RSV viral glycoproteins have also been shown to be safe, and a third subunit vaccine has just completed initial evaluation (56-58). Live, attenuated vaccines may be the most promising approach for protecting infants and children against RSV infection, since they can be administered by the natural route of inoculation (nasally) and should induce an immune response similar to natural infection. Live, attenuated vaccines can replicate in the presence of maternal antibodies; therefore, immune responses should be good during the first 6 months of life, when protection is most needed (55). Live vaccines in the form of oral or nasal sprays may be particularly well-suited for use in remote areas because they do not require injection and could potentially be administered by parents.

RSV infections have a tremendous health impact on an individual and societal level. An effective RSV vaccine could result in reductions in hospitalizations, otitis media and chronic respiratory diseases in children. Until such a vaccine is available we will need to focus on other preventive measures such as encouraging breast feeding, and teaching families about the importance of good handwashing and not to share cups or utensils with ill persons. Parents who smoke should be warned about the health hazards their children face due to continued exposure to smoke. Additionally, because RSV causes between 14,000 and 62,000 hospitalization for pneumonia in the elderly in the U. S. each year, prevention research and vaccine development should not be focused on children only (6).

In Alaska, we face unique problems from the high rates of RSV infections and their sequelae and should be ready to take up the challenge to explore new methods of preventing and controlling this disease. Alaskans could benefit greatly from the early introduction and evaluation of a promising new vaccine should one become available, and careful consideration should be given to future opportunities to participate in vaccine trials. Additional work is required to better understand the reasons for the high rates of RSV infection in Alaska and to determine the burden of RSV disease in elderly Alaskans. The contribution of indoor air pollution from cigarette or other smoke needs further evaluation. The combination of high rates of cigarette smokers and the common use of poorly vented wood burning stoves as heat sources may pose a double threat to small children in many households. Finally, continued monitoring of RSV illness and the long-term sequelae of RSV infection among Alaskans is vital for developing effective methods for preventing debilitating chronic lung diseases.

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(continued on page 101)

From Out of the Past — Over 30 Years Ago

Gloria K. Park, MD

Frontier Medicine in SE Alaska

Harry Carlos DeVighne, MD

9/3/1867 – 8/7/1957

Born in Havana and orphaned at a young age in New York City. Joined an 1884 political parade, found a friend and deserted his foster home. The friend died so Harry grew up on the streets of NYC mainly as a newsboy until a truant officer put him on a train to Iowa to a foster home on a farm where he did attend about 4 years of school. He then left by train to find a foster uncle and study law with him in Deadwood, South Dakota but instead became a hobo, working many odd jobs across the USA. Even worked on a cattle ship to Liverpool and on a gun-runner to Cuba. Tried to join the Rough Riders in San Antonio but arrived there a day late. Earlier he had met a physician in St. Louis and started reading any medical books he could find, e.g. "Dr. Warren's Household Physician". Found a job as a medical student in San Antonio in a large new state hospital. Worked as a male nurse and pharmacy assistant and continued to study. Got a reference to a medical school in San Francisco for $200 a year tuition (name of school unknown). Graduated $100 in debt and started an internship at the City and County Hospital but not an official paying position. He soon heard of an opening at the Good Samaritan hospital in Portland, Oregon where he earned $15 per month plus board and room. In 1904 he was offered a job in Alaska by the US Bureau of Education for $150 per month and travel expenses. He had 55 cents in his pocket when he boarded the ship at Seattle en route to Wrangell.

The preceding information is from "*The Time of My Life*", his autobiography, published in London, 1946. Following are excerpts from his book and pictures from the "Alaska Journal", Vol 14, No. 2 of 1984. Thus his 30 year career in Alaska is depicted in his own words. He was Secretary-Treasurer of the Territorial Board of Medical Examiners for 20 years and served as Territorial Commissioner of Health for 12 years. He spend two years in the US Medical Corps during WWI. He worked in Wrangell, then Douglas and moved to Juneau in 1915. He moved to California in 1934.

"There was but one vacant house in a good location, a rough board and batten structure about ten by twenty feet in size with a partition dividing it into two equal parts, one room furnished with an old rusty stove, the other with a home-made table, chair and stool. I tried the stove, which smoked furiously, then threw out a generous amount of heat. Fortunately for the preservation of my enthusiasm, I did not realize that ice and snow had sealed the roof; that when they melted a large part of the resultant water would drip through.

"Out of empty boxes I made shelves, arranged my instruments and supplies with the idea of showing them to good advantage. The mayor-postmaster-hotel-keeper was interested and helpful, lending me a good lamp for my surgery, another lamp and a chair for my reception room, various articles I could use. He told me later he knew by the gleam in my eyes that I meant business and he suspected I was broke. In this latter he was absolutely wrong; I still possessed the five cents with which I had landed.

"On the fourth day after arriving I brushed out the last speck of dust, arranged for the last time my visible stock-in-trade, sat down in my one good chair to appraise the effect and to pronounce it good. I was ready for my first patient.

Wrangell as it appeared during Dr. Harry De Vighne's residence there after 1904.

(Courtesy of the Alaska Historical Library)

"She slid halfway into a chair, folded her hands demurely and murmured, 'It's my leg. It's been sore a long time, and it hurts when I stand still.'

"I imagine few sore legs have been examined more closely or with greater concern, that rarely has a simple varicose ulcer been treated with such respect and thoughtfulness; after alternately dabbing it with cocaine and scrubbing it with green soap, I applied an ichthyol dressing under a tight adhesive bandage. I was so completely absorbed in my work, and in explicit directions for after-care, that when she asked the amount of my fee I was momentarily taken aback.

"'One dollar and sixty-five cents,' I managed to reply, whereupon she counted out the exact change. How or why this odd figure occurred to me is one of the small mysteries still unsolved; but the ulcer healed. . . at the end of my first month's practice I had made and collected nearly fifty dollars. The next month I collected more than a hundred. The practice of medicine was justifying my most sanguine expections.

"In the early nineteen hundreds the only law in Alaska applicable to the healing art, enacted for the territory by act indifferent Congress, but not even indifferently enforced, provided that to procure a license to treat the sick one must possess a diploma from a medical school and pay a five-dollar recording fee. No one bothered to inquire whether the diploma was front a reputable institution, or whether it had been earned, bought, stolen, or, in fact, whether or not it was a medical diploma. I ran across one undaunted practitioner whose sole credential upon which he based his professional claims was an imposing-looking certificate of membership in a lodge. As a result medicine in Alaska was represented by a variety of talent, some of which was disreputable and more of it decidedly questionable.

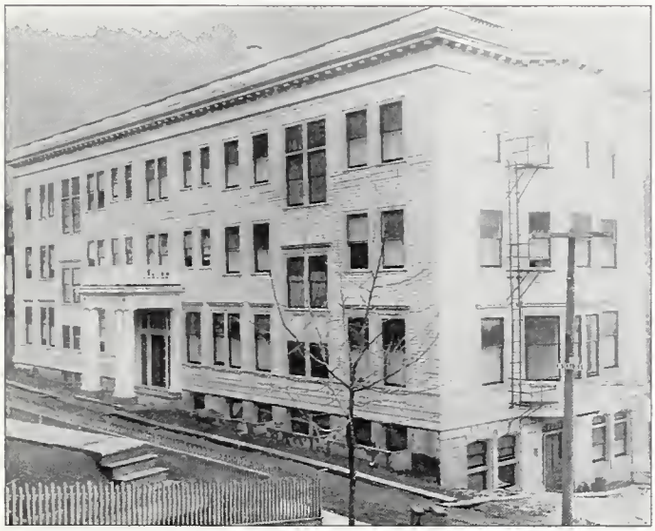
"A small hospital had been established in each of the seven largest centers of population, located from two to five hundred miles apart and boasting, optimistically, of from two to three thousand inhabitants each. About twenty doctors were practicing in the larger communities, and perhaps a half-dozen medical missionaries were scattered throughout the territory. But scores of smaller towns containing up to a thousand people had no medical service of any kind. It was for the purpose of visiting and inspecting these isolated settlements, relieving such illness as I found and recommending methods designed to improve the general state of health, that my commission was issued by the Bureau of Education.

The hospitals in Alaska were far more primitive than those in New York City, where De Vighne went to do graduate work. This room in Saint Ann's Hospital in Juneau was equipped with a wood stove and a coal oil lamp.

(Sisters of Saint Ann, reprinted from *The ALASKA JOURNAL*®)

"My equipment was a regulation U.S. Army medical chest supplementing another chest of emergency supplies, a folding cot, blankets, extra clothing, a modicum of medical knowledge and a determination to make good. The region to be inspected extended from the southern boundary of Alaska to the farthermost Aleutian Island; transportation included anything available from regular passenger steamships and revenue cutters down to native canoes. More than a hundred villages were visited; more than five thousand natives were given physical examinations, or treatment, or both.

"Travelling *de luxe* on passenger steamers and revenue cutters was a pleasant way to enjoy Alaska's magnificent scenery and appreciate its vast extent, but it was no way to learn what I wanted to know about the natives. On my personally conducted tours of the villages I saw only what my escorts wanted me to see, met only those with whom they wanted me to talk, and learned only what they themselves had known for years. My notes from which reports to the Bureau



Saint Ann's Hospital in Juneau where De Vighne delivered his one thousandth baby in March 1920.

(Courtesy of the Alaska Historical Library)

were made showed the circumstances under which the natives lived, the chief causes of death, the number in each village afflicted with various diseases, and the kind and amount of services I had rendered. This was chiefly medical, but often included more than pills and potions. I pulled hundreds of teeth, dressed dozens of wounds, incised numerous abscesses, and delivered several babies, one quite unexpectedly in a canoe several miles from shore and another under a tree on the beach.

"In summer a small, easily discouraged steam ferry made the crossing and returned at two-hour intervals from early morning until midnight, weather permitting. Aside from loss of time and a mile walk to and from the dock, this was no great affliction; the half-hour voyage was a restful interlude in a busy day. But in winter, which began in early September and ended late in May, to make the round trip on schedule was a feat in which sheer luck played no small part.

Furious gales then swept down between two high mountain ranges, driving sheets of icy spray before a white-capped, choppy sea with breath-taking velocity, while incoming tides and subzero temperatures often all but blocked the channel with icebergs and coated every exposed surface with ice. At these times the ferry, being unable to run, simply waited behind a protecting wharf until the storm abated; passengers remained at home or on the other side, as chance and weather ordained.

On one occasion, after taking a patient across to the hospital and standing by until her baby was born, I found myself stuck there for three days, which I improved by giving her more personal attention than any woman had need or reason to expect; as a matter of fact, I spent most of the time in the hospital. When the storm had apparently spent itself, ten stranded and disgruntled passengers boarded the ferry, only to have it sink beneath them when its lines were cast off. Another boat was substituted, encrusted ice was chopped off the deck, a feeble fire slightly warmed its cabin, and again we climbed aboard. We succeeded in crossing, but when tile engine was slowed down to make a landing it stopped dead; strong offshore squalls carried us past the dock and on down the channel. Seven miles below town we fetched up on the beach; all of us got ashore, wet and cold, but safely. Someone started a fire; to keep from freezing, everyone, including three women, worked furiously carrying driftwood until the exertion and the fire warmed us thoroughly. A dog-team came down, picked up the women. The rest of us walked in; after a hot drink, dry clothing and a good dinner, none was worse for the experience.

Three years later, in 1915, we moved across the channel to Juneau, then claiming a population of two thousand inhabitants. In appearance it differed in no important respects from Douglas or Wrangell.

Year by year we watched, and to some extent participated in, the transmutation of this small, ugly mining camp into a bustling little city, the capital of a domain in area one-fifth that of the continental United States. Its muddy streets were paved, two and three-storied concrete buildings replaced its wretched shacks and false-front stores. The old Treadwell gold-mine caved in, but the Alaska-Juneau developed a bigger one at the edge of town. The Federal Government rediscovered Alaska, its neglected stepchild, and while still dizzy with astonishment erected a million dollar Capitol building, a large hospital for natives, a mile-long bridge across the channel. This called for modern apartment houses and an ultra-modern hotel, where second-generation pioneers could dunk their morning doughnuts at a mahogany counter, and of an afternoon gather with the ladies in a luxuriously appointed cocktail lounge

Heretofore we had relatively few patients whose ailments and disabilities were not clearly manifest. Our practice was made up largely of wounds and injuries due to external violence, exposure to the elements, nutritional disorders and their complications, along with diseases and constitutional defects recently brought into the territory. Functional diseases among the old-timers were rare; neurotics had something more vital and pressing to worry about than their neuroses. But changes were creeping in upon us, stresses and strains on overwrought nerves and overworked bodies were taking their tolls. I recall a middle-aged, high-pressure executive not long in the country who came into the office complaining of a peculiar pain in his chest. While I was

The U.S. Government Hospital in Juneau, where De Vighne treated many of his native patients.

(Courtesy of the Alaska Historieal Library)

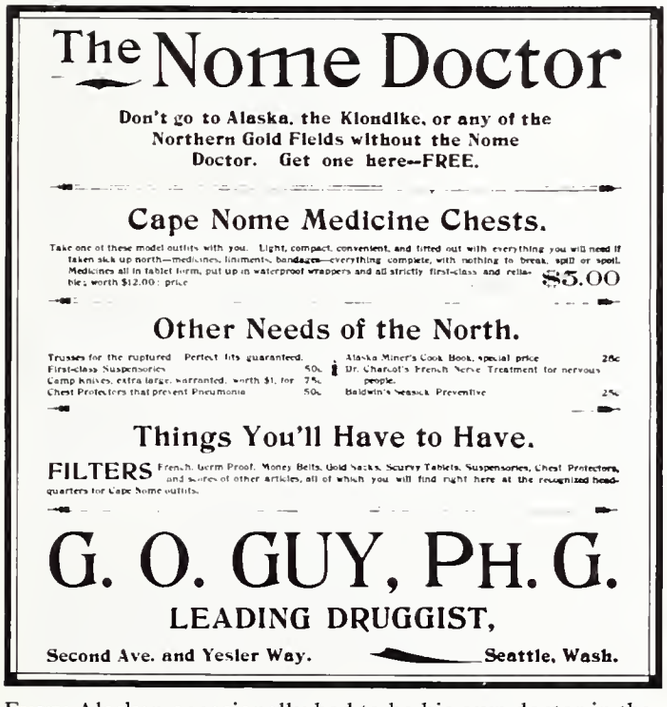
reaching for my stethoscope he stopped talking, clutched at his shoulder, then froze into immobility, while a ghastly expression of pain and alarm spread across his face. An instant later he collapsed to the floor, and I had a rare opportunity to hear the last faint sounds of a heart stopping irremediably by a coronary occlusion.

Scarlet fever appeared, and typhoid, and I saw my first case of diphtheria. Four years later, in Nome, the first epidemic of that dread disease was reported; as Territorial Commissioner of Health, it was my job to have a half-million units of antitoxin delivered to the stricken town. Midwinter storms were raging over the northland, with temperatures down to minus forty degrees or more. There was only a few thousand units of serum in the territory; a supply must be ordered from Seattle. This was shipped to Fairbanks, repacked against freezing, and carried from there to Nome by relays of dog-teams travelling day and night over unmarked trails. The trip was made in a few hours less than five days, an all-time record. Regular dog-team mail service between Fairbanks and Nome then required three weeks; the regular time by plane is now seven hours.

The hospital doubled its capacity, giving us four wards, twenty private rooms, eighty beds. We now had a fully equipped laboratory and X-ray department, an up-to-date surgery, a corps of well-trained nurses. Alaska's real pioneers were the Sisters of St. Ann. Long before the gold-rush, when the country was thought to be a frozen, ice-bound wilderness, these devoted and indefatigable trail-blazers were establishing mission schools and rudimentary hospitals where those who followed later could find healing care and sanctuary. Necessarily, these Sisters possessed qualities of courage and adaptability far above the average, and an inflexibility of principle and purpose which could not be broken, nor even bent. Through many years of close association me to realize this fact and to govern myself accordingly.

My first automobile bore an intriguing license plate, Alaska-2, which gave rise to several anxious moments when I shipped it to Seattle and drove to New York. Though I had never driven in traffic and was unfamiliar with its laws and regulations, the trip presented no great difficulties. In fact, there was nothing to it. Proceeding leisurely over the southern route, we passed through the smaller cities in the early morning, hours, skirted Washington and Baltimore, negotiated the Holland Tunnel, headed up Sixth Avenue one Saturday morning about eleven o'clock. Never had I believed the city I thought I knew so well could be so nerve-racking: a narrow street, two surface railways, an elevated, dozens of honking taxis, hundreds of rumbling trucks, thousands of quite mad pedestrians, all seemingly bent on saluting the first Alaska car they had seen.

It was tough going. After two weeks of quiet country driving the racket was deafening. In every block someone hopped on the running-board to have a look at the Eskimos, to ask questions I had neither time nor disposition to answer. At Thirty-third Street



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Every Alaskan occasionally had to be his own doctor in the early days. This was an advertisement for a medicine chest sold during the gold rush. De Vighne encourntered several seriously injuried individuals who had treated themselves and managed to survive. (Courtesy of the University of Washington Library)

The license plate on Dr. DeVighne's first automobile said Alaska-2. He caused a stir when he drove his car – without a driver's license – through New York City. This photo of a traffic jam in Juneau was taken in the early 1950s, by which time many Alaskans had their own automobiles.

(Courtesy of J. Malcolm Greany)

a mounted policeman edged us over to the curb, dismounted, rested his arms on the door while looking us over.

"So you're from Alaska, hunh? Long way from home, I'd say." His voice rasped ominously, serving to open my pores for a flow of clammy perspiration. "Where you goin'?"

Murmuring something about the City Club on Forty-fourth Street, I tried to look unconcerned. But I had no driver's license—such protective measures had not yet reached Alaska—nor had I a certificate of car ownership. In the north none was necessary. Worse still, in the back of the car was a two-gallon keg of Kentucky "corn," picked up at a moonshiner's cabin near Jenkinsville.

In the circumstances neither my wife nor I was possessed of much composure as the officer fished in a pocket, began scribbling on a card. In those days of "Noble Experiment" the discovery of my contraband would certainly lead to complications.

"All right, Skipper," said the officer, finally. "Straight ahead about ten blocks, then turn right. An' send me a pretty postcard when you get back to Alaska, will you? I'm making a collection."

We returned home without serious mishap. I mailed the policeman his postcard.

Among the first Acts of the Alaska Legislature two were of especial interest to me: one providing for registration of births, deaths and marriages, the other creating a Territorial Board of Medical Examiners, of which I served as Secretary for twenty years. This law closed the last open door to unrestricted medical practice within the jurisdiction of the United States. Only eighteen doctors then practicing in the territory were found to be eligible for license under the new law's provisions, all of them general practitioners, and all qualified to render acceptable medical service

Pioneer medical practice is always rich in priorities. In any given locality where there has been no adequate medical service the chance to be first to do something, however unimportant, amounts to certainty. This was so in old Alaska, where I believe I was first to perform a successful Caesarian section upon my first attempt; to use the newly discovered 606 in syphilis; to induce twilight sleep in obstetrics with scopolamine and morphine; to use pipe-cleaners wrapped in gauze as surgical drains; to catheterize a woman with a cigarette-holder sterilized in kerosene; to make serviceable moulded splints with gauze dipped in flour paste; to cultivate a strain of pure streptococci from what was locally known as fish-poisoning; to pull sixty-odd teeth before breakfast in an Indian village, my patients sitting on a convenient rock.

No one, so far as I know, preceded me in losing twenty-one dollars on four aces in a penny ante, ten-cent-limit poker game; or in charging a millionaire one hundred dollars for incomplete hysterectomy on his wife and have him kick at the cost; or repairing the stump on a man who had amputated his own foot, caught four days before in a bear trap; or treating five cases as chicken-pox and discovering, when one died, that the disease was smallpox. Nor had anyone previously brought healthy twins, or siblings, into the world three days apart, or delivered a baby in the Governor's mansion, another in an Indian canoe five miles from shore, another in a Ford, another in an office waiting-room."

Dr. De Vighne in his office. He delivered about three thousand babies during his career, including the dozens of children whose pictures are on the wall.

(Courtesy of Dana D. Kupelian)

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Editorial. . .

William R. Clark, MD

This last 20th Century issue and first of the 21st Century has delivered us past the dreaded computer collapse based on Y2K terror. Our world and Alaska face many more real challenges. One arena is certainly the fiscal gap that we, as opposed to the Lower 48, face in these declining and realigning days of oil field production. As we physicians have limited input into these matters, one can only hope that adequate and accurate information is available on which to base our State's direction. In the medical community where we do have more say a recent shift in direction has become more and more apparent. The rather rapid trend away from the primary care gatekeeper model to a specialty-directed system. This has great implications for Alaska as we have duel enemies to conquer. First, geography continues to be a problem. A solution may be the remote medicine/telemedicine project that continues to expand – now with multi-agency support. We are a proving ground for this technology not just for the nation but also in the global community. Upcoming seminars such as the Internet Telemedicine Symposium at Providence are good places to start learning more. Entreprenial opportunities can be found in any profound shift in delivery systems and we must, and will, need a voice in these decisions. These technologies portend a new and greater challenge to our society and our standards of practice.

A second new problem looms before us here and in the country as a whole. The movement to demonstrate that allied health providers, i.e. PAs, PNPs, even pharmacists can act as equivalent substitutes for physicians (JAMA, Jan 5). This also does not bode well for the future of a new Family Practice emphasis. Paradigm shifts in either our support or orientation of future WWAMI and resident-training programs should be considered or soon our delivery system will be decidedly altered in our abstention. Our medical society is still our strongest voice in these regards but other avenues may be required. How we relate to these allied movements will influence our working relationships and the patient/provider relationships for years to come.

We at *Alaska Medicine* continue to try to find ways to better serve you and you in turn, please do not hesitate to give us your suggestions. We appreciate your support. JAMA, Vol 283, No. 1, pg 59-68

(continued from pg 93 - Respiratory Syncytial Virus)

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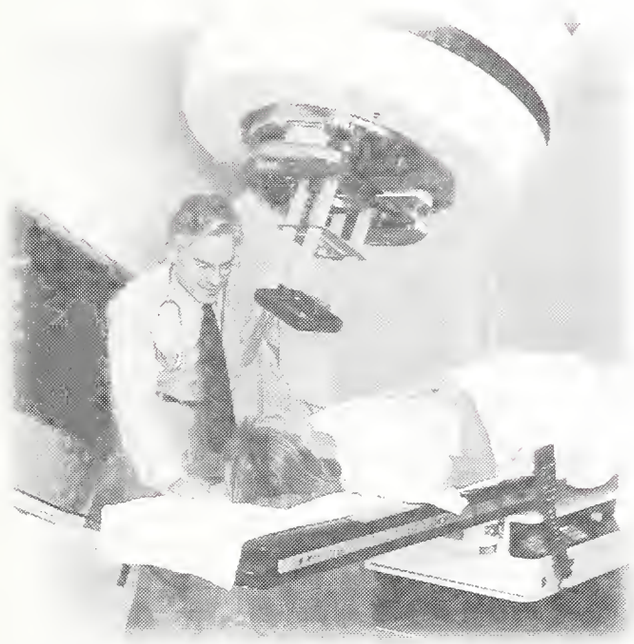

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